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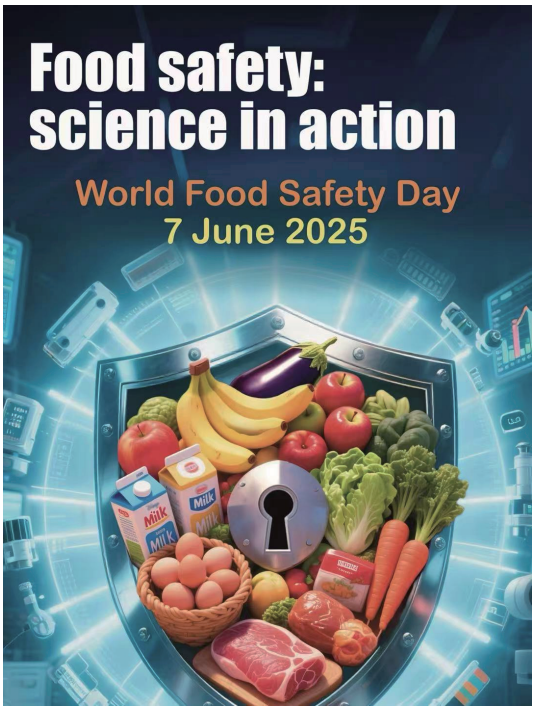

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Perspectives

The Concept and Scope of Resilience Against Infectious Disease Outbreaks

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ABSTRACT

Resilience is widely discussed and applied across multiple disciplines, with its concept having evolved in the field of hazards and disasters over recent decades. However, there remains a lack of a resilience concept specifically applicable to infectious disease outbreaks, which can lead to misidentification of key issues in outbreak prevention and control, hindering the effective application of this concept. This study aims to provide a clear definition of resilience against infectious disease outbreaks. Building on the fundamental meaning of resilience and its application to hazards and disasters, the research has identified and developed several essential elements for resilience against infectious disease outbreaks by comparing infectious diseases with other types of natural hazards. This study then proposes that resilience against infectious disease outbreaks is the capacity to effectively prevent, detect, respond to, and control outbreaks without seriously affecting essential functions of health and social systems, which could be measured by the intensity of infectious diseases that an area can effectively manage. The concept and scope of resilience proposed in this study provide a valuable framework for improving regional capacity to better prepare for potential epidemic and pandemic threats in the future.

Resilience has become an attractive and widely discussed concept across multiple disciplines (*1*). Before evolving into its diverse contemporary applications, resilience originated in 19th-century material sciences as a purely mechanical concept, referring to an object's elastic recovery capacity and its maximum recoverable deformation after exposure to external forces (*2–3*). Since the 1970s, fields including ecology (*4–5*), psychology (*6*), and sociology (*7*) have developed discipline-specific understandings of resilience.

As natural disaster frequency has substantially increased in recent decades (*8*), the international community and disaster management researchers have recognized the importance of reducing natural hazard risks and building disaster resilience (*9–12*). The concept has become mainstream in addressing complex disaster risk challenges (*13*). Research on resilience to hazards and disasters has explored a broad range of potential threats and their consequences. While some studies focus on resilience to generic natural hazards, others examine specific hazard types, with meteorological and geological events such as floods, earthquakes, and hurricanes receiving the most attention. Public health crises, however, have received comparatively limited consideration (*10,14–15*). In these studies, resilience is typically described as a system's ability to absorb, accommodate, or recover from hazardous events while maintaining acceptable functioning and structure (*8–9,16–18*). This conceptualization applies particularly to hazards and disasters that are difficult to prevent and cause substantial short-term damage to infrastructure and social systems.

With the increasing threats of emerging infectious diseases (EIDs) since the 21st century, including severe acute respiratory syndrome (SARS), pandemic influenza (H1N1) 2009, Ebola, and the coronavirus disease 2019 (COVID-19) pandemic, resilience has been identified as a critical concept for addressing complex public health crises in countries, communities, and health systems in novel ways (*19–20*). An increasing number of studies have explored resilience in the context of social systems or health systems facing public health crises (*21–29*), largely following the understanding of resilience developed for hazards and disasters.

Infectious diseases and outbreaks differ significantly from other natural hazards and disasters in their impact patterns and response processes. Ignoring these differences results in a lack of appropriate resilience concepts for infectious disease outbreaks, which can misdirect attention from key issues in outbreak

prevention and control, hindering effective application of the resilience concept. There is an urgent need to develop a specific understanding of resilience applicable to infectious disease outbreaks.

Comparison Between Infectious Diseases and Natural Hazards

We compared the characteristics of infectious diseases and outbreaks with other commonly studied natural hazards and disasters in resilience research, including earthquakes, floods, and tropical cyclones, to illustrate the distinctions between them in several categories (Table 1). According to the crisis life cycle (*30*), we identified three categories: "*prevention and preparedness*", "*emergency response*", and "*recovery and reconstruction*" with nine sub-categories that represent aspects of prevention and response to hazards and disasters.

The comparison revealed several key distinctions between infectious diseases and other hazards (*8*,*31*–*33*), indicating that resilience against infectious disease outbreaks should not directly adopt disaster resilience frameworks. First, most natural hazards and disasters cannot be directly intervened in or altered, and losses can only be reduced through preventive preparations before the disaster and rapid rescue afterward (*34*). In contrast, infectious disease outbreaks allow for a shift from reactive response to proactive measures (*33*), with key emergency responses focusing on appropriate non-pharmaceutical interventions (NPIs) based on understanding the epidemiology and transmission dynamics to control outbreak spread. Second, disasters caused by natural hazards are often destructive, resulting in substantial infrastructure damage, injuries or loss of life, and disruption of social order and economic systems, requiring significant post-disaster recovery and reconstruction. However, local infectious disease outbreaks can often be managed early through routine prevention and control measures, with limited impact on social life (*8*,*34*). Third, while epidemics or pandemics may impact infrastructure and social systems, they are not inherently destructive (*35*–*36*), thus eliminating the need for post-disaster infrastructure reconstruction.

Aspects that Need to Be Emphasized for Resilience Against Infectious Disease Outbreaks

Based on the similarities and differences between infectious diseases and other hazards, as well as our understanding of resilience to hazards and disasters, we propose several key aspects that should be emphasized to clarify resilience applicable to infectious disease outbreaks. The connections and distinctions between resilience against infectious disease outbreaks and the general understanding of resilience in the field of hazards and disasters have been summarized in Table 2.

TABLE 1. Comparison of infectious diseases with common natural hazards and disasters.

Categories	Sub-categories	Hazards characteristics		
		Earthquake (geological)	Flood, tropical cyclone (hydro-meteorological)	Infectious diseases (biological)
Prevention and preparedness	Controllability of risk occurrence	Uncontrollable	Uncontrollable	A certain degree of controllability
	Accuracy of monitoring and warning	May not be accurate	Relatively accurate	Routine outbreaks: relatively accurate; EIDs: inaccurate
	Time from warning to response	A few or tens of seconds	Several days	A few days or more
Emergency response	Disaster intervention	Unable to intervene	Unable to intervene	Interventions are key response measures
	Protection of population and reduction of losses	Evacuation, emergency rescue, medical treatment	Protective measures in advance, emergency rescue, evacuation, medical treatment	NPIs, vaccine development and emergency use, medical treatment, etc.
Recovery and reconstruction	Impact on people	Injuries or loss of life	Injuries or loss of life	Harmful to health and may cause death
	Impact on infrastructure	May be destructive	May be destructive	No significant impact on infrastructure
	Impact on social and economic	May cause disruption of social order, economic losses	May cause disruption of social order, economic losses	Large-scale outbreaks can have some impact on social life and the economy
	Need for recovery and reconstruction	Usually required	Usually required	May include recovery; reconstruction not required

Abbreviation: EIDs=emerging infectious diseases; NPIs=non-pharmaceutical interventions.

TABLE 2. Connections and distinctions between resilience to disasters and resilience against infectious disease outbreaks.

Elements	Resilience to hazards and disasters	Resilience against infectious disease outbreaks
Connections		
Primary sense	The ability to withstand external pressures	
Content	Well-prepared, risk identification, remaining functional under extreme stresses, and recovery	
Distinctions		
Research scope	Regions/social or health systems	Including health systems and participants from communities and social systems when the outbreak exceeds the routine level
Dimension: core capacity	Remaining functional under extreme stresses; recovered and re-established from the effects of hazardous events	Proactive response and control; dynamic control strategies adjusted by local capacity and outbreak levels to maintain functions of health systems and social systems
Dimension: external pressure	Extreme events and disasters that would cause much damage to infrastructure and social systems in the short term	Infectious diseases with incubation periods that can escalate to different levels of outbreaks and can be controlled by public health measures.
Critical point	The limit to remaining functional under extreme stresses	*The switching point:* the critical values of shifting from the condition of daily outbreak response to the emergency response; *the resilience threshold:* the point at which outbreaks reach the maximum intensity that can be handled within the capacity of an area

Proactive response and control While most natural disasters cannot be controlled and occur suddenly with large-scale impacts in a short period, resilience to disasters emphasizes an area's ability to passively withstand, recover, and reconstruct to minimize socio-economic losses. In contrast, infectious diseases with high epidemic potential typically have incubation periods and transmission processes that allow for a relatively long intervention window after early warning. Measures targeting the source of infections, interrupting transmission routes, and protecting susceptible populations (*37*) can be implemented according to the transmission patterns and dynamics of infectious diseases to contain outbreaks before they escalate to larger scales and impact communities.

Outbreak response strategies should be aligned with local capacities An area's capacity determines the extent of outbreaks it can effectively control. Areas with sufficient resources and strong capacities can manage outbreaks using existing infrastructure for extended periods, while vulnerable areas with capacity limitations require more stringent measures to maintain basic functions and avoid rapidly exceeding local capacity during outbreaks. Resilience against infectious disease outbreaks encompasses multiple capacity dimensions beyond health systems alone. The capacities required differ between daily outbreak response and emergency response conditions. Generally, capacities related to resilience against infectious disease outbreaks include the professional expertise of local disease control and prevention agencies, resource reserves and utilization, surge capacity of health facilities, multisectoral cooperation, and community engagement.

Rapid recovery and improvement Negative impacts on health and social systems can be minimized if interventions are implemented effectively during the early stages of outbreaks. While restoring health facility functions and resuming social activities is necessary once large-scale outbreaks are controlled, this recovery process is relatively rapid compared to recovery from other types of disasters. Furthermore, since outbreaks typically do not cause substantial damage to infrastructure, post-outbreak efforts should focus on addressing weaknesses in health systems to better prepare for and prevent future pandemics, rather than reconstructing buildings and facilities, which is often emphasized in disaster resilience.

Concept and Scope of Resilience Against Infectious Disease Outbreaks

Building on the aspects that should be emphasized for resilience against infectious disease outbreaks, resilience against infectious disease outbreaks can be defined as the capacity of an area to effectively prevent, detect, respond to, and control outbreaks without seriously affecting essential functions of health and social systems. The largest outbreak intensity that an area can cope with indicates the upper limit of resilience against outbreaks, which can be recognized as the resilience threshold.

The capacity of an area to cope with infectious disease outbreaks determines the maximum degree of outbreaks that the area can withstand, forming the

scope of resilience against infectious disease outbreaks. Under the condition of daily outbreak response, the required capacities mainly include the basic skills for disease control and prevention at the local level, timely detection and reporting of infectious disease cases of unknown origin at all levels of healthcare institutions, emergency response planning, resource reserves, and other preparations for epidemics and pandemics. Under the condition of emergency response against a large-scale outbreak exceeding the daily level, advanced professional skills, utilization of redundant resources, and surge capacity of health facilities are required. Once the outbreak level exceeds the capacity of local agencies for disease control, coordination of actors within and outside health systems is often needed in addition to other capacities. Depending on the scale of outbreaks, reflection on lessons learned and continuous improvement of overall capacity are also required once the outbreak is under control.

Since routine outbreaks can be controlled through daily operations by local agencies, building resilience against outbreaks should focus on capacities to control outbreaks that exceed daily levels. These large-scale outbreaks put pressure on local capacity and require emergency response with the utilization of reserved resources. The threshold of resilience against infectious disease outbreaks in an area is likely determined by the weakest critical component of its prevention and control capacity.

Based on the above understandings, resilience against infectious disease outbreaks can be represented by a schematic (Figure 1). The horizontal axis represents the outbreak prevention and control capacity of areas, while the vertical axis represents the intensity of infectious disease outbreaks over time. The capacity of each area determines the upper limit of outbreaks that can be handled in that area, resulting in the corresponding level of resilience. The curve of *Resilience thresholds* represents the critical values of the maximum intensity of outbreaks that can be handled within the capacity of areas, and the curve of *Switching points* represents the critical values of shifting from the condition of daily outbreak response to the condition of emergency response in areas. The schematic illustrates a possible changing pattern of resilience against infectious disease outbreaks in areas with different capacities.

Discussion and Conclusions

By inheriting the fundamental understanding of resilience and developing the concept of disaster resilience based on the characteristics of infectious diseases, this study proposes a concept and scope of resilience specifically applicable to infectious disease outbreaks. This framework provides valuable insights for addressing critical issues related to outbreak prevention and control, and can guide preparation and response strategies in different regions, highlighting the importance of resilience in infectious disease management.

The concept of resilience against infectious disease outbreaks proposed in this study focuses on acute

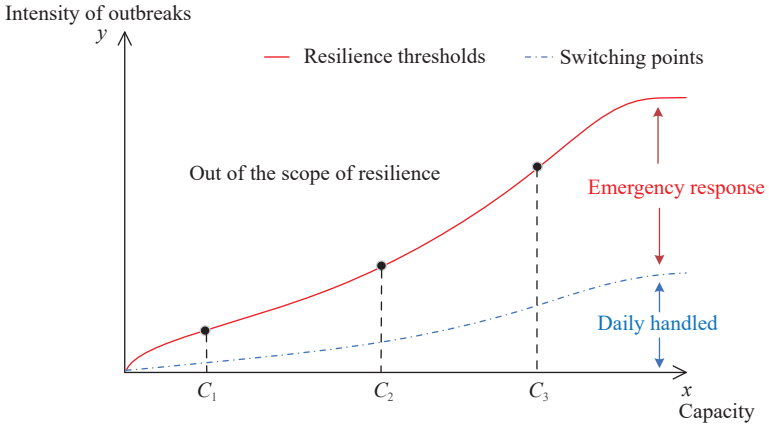

FIGURE 1. Schematic of resilience against infectious disease outbreaks.
Note: 1) *x* is the outbreak prevention and control capacity, and *y* is the intensity of infectious disease outbreaks over time. Capacity determines the intensity of outbreaks in a certain period that can be handled in an area. 2) The curve of *Resilience thresholds* represents the critical values of the maximum intensity of outbreaks that can be handled within the capacity of areas, and the curve of *Switching points* represents the critical values of shifting from the condition of daily outbreak response to the condition of emergency response in areas. C_1, C_2, and C_3 represent regions with different capacity have corresponding levels of resilience thresholds and switching points.

infectious diseases that can cause sudden onset and large-scale outbreaks in the short term, regardless of their transmission routes (airborne, vector-borne, direct contact, etc.). Diseases with high transmissibility or virulence, such as SARS, COVID-19, and Ebola, pose the greatest threat to resilience because they can rapidly overwhelm local health systems, leaving insufficient response time. These diseases require comprehensive capacity and redundant resources to prevent epidemics from exceeding the upper limit of local resilience. In July 2024, the WHO launched a pathogens prioritization framework (*38*) for epidemic and pandemic research preparedness, which can help clarify which diseases should be prioritized to enhance global resilience against epidemics and pandemics, though priorities may differ when adopting a regional perspective.

Our findings provide insights into resilience against infectious disease outbreaks, aligning with the WHO's recommendation to further explore and understand the application of resilience to various health system challenges (*39*). The WHO's recent reports (*40–41*) define a framework for health system resilience against diseases and other events that is consistent with our overall concept. However, the WHO's framework encompasses both acute and chronic diseases and provides general capacity requirements for health systems across countries with varying development and economic conditions. In contrast, our concept specifically addresses resilience against acute infectious disease outbreaks and integrates the temporal intensity of outbreaks with the capacity of local health systems and other stakeholders. Additionally, we developed specific capacity elements for resilience against outbreaks primarily in the context of China's health systems. Similar distinctions exist between our approach and Nuzzo's study (*24*). The advantage of this study's concept is that it considers the dynamic nature of epidemics relative to regional capacities, providing a framework for measuring resilience against infectious disease outbreaks across different areas. Unlike Zhao's study (*42*), which measures resilience using indicator system scores, our proposed resilience threshold allows regions to identify specific capacity shortcomings that limit their ability to manage outbreaks, enabling more targeted improvements rather than applying uniform standards across different regions.

Redundancy and resourcefulness are key attributes for pandemic preparedness (*43–44*) and are recognized as important "means" of resilience to natural hazards and disasters (*45–46*). Resilience against infectious disease outbreaks should be assessed proactively to ensure adequate redundant resources and appropriate mechanisms for resource utilization and deployment. Based on their resilience capacity, regions can develop and revise contingency plans for outbreaks of varying intensity; authorities and agencies should establish mechanisms for transforming public health strategies and allocating redundant resources to effectively implement interventions that can withstand large-scale outbreaks and potentially long-lasting pandemics.

For infectious disease outbreak prevention and control, the resilience threshold has a unique meaning that differs from the ecological resilience threshold (*47–48*). It represents the point at which an outbreak reaches the maximum intensity that can be managed within a region's capacity. When this threshold is exceeded, the outbreak has caused widespread transmission beyond the region's capacity to control, which can seriously affect health and social systems, resulting in significant costs. Support from other regions and implementation of strict public health and social measures become necessary. Therefore, a region should assess its resilience threshold in advance and take measures to avoid exceeding it during epidemics and pandemics.

In conclusion, resilience requires specific definitions tailored to different fields to be effectively applied. Based on the understanding developed in this study, the exact scope and elements of resilience against infectious disease outbreaks at local and regional scales can be further defined. This will guide regions in implementing appropriate measures for different outbreak levels, achieving overall capacity improvements, and enhancing their sustainability against large-scale outbreaks while better preparing for future pandemics.

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Vital Surveillances

An Increasing Prevalence of Non-GII.4 Genotypes Causing Norovirus Gastroenteritis Outbreaks — Beijing Municipality, China, 2017–2024

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ABSTRACT

Objectives: Since 2014, non-GII.4 norovirus genotypes have increasingly challenged the predominance of GII.4, particularly in Asia. This study analyzed the epidemiological and genetic characteristics of norovirus outbreaks from January 2017 to June 2024 in a district of Beijing, China.

Methods: We tested 2,016 stool samples collected from 309 acute gastroenteritis outbreaks for norovirus using real-time RT-PCR. Partial polymerase and capsid sequences of norovirus-positive samples were amplified and sequenced for phylogenetic analysis. Additionally, we performed genome amplification and sequence analysis on seven GII.7[P7] strains.

Results: Between January 2017 and June 2024, 150 norovirus outbreaks were reported, with GII norovirus causing 83.3% of these outbreaks. We identified 16 distinct genotypes. Among the 102 GII genotype outbreaks, non-GII.4 norovirus outbreaks (81.4%) significantly outnumbered GII.4 norovirus outbreaks (18.6%). The three most prevalent genotypes during the study period were GII.2[P16] (46.1%, 47/102), GII.3[P12] (14.7%, 15/102), and GII.4 Sydney[P16] (12.7%, 13/102). GII.2[P16] predominated in 2017, 2018, and 2020, while GII.3[P12] was the dominant genotype in 2022. Multiple genotypes emerged in 2023. In the first half of 2024, GII.4 Sydney[P16] became predominant (36.9%), while a novel GII.7[P7] variant emerged, accounting for 26.3% of outbreaks. All seven GII.7[P7] genome sequences formed an independent branch in both VP1 and polymerase regions.

Conclusions: Our findings demonstrate that non-GII.4 noroviruses play an increasingly important role in outbreaks in Beijing. Continuous surveillance is needed to better understand and control norovirus outbreaks in future epidemic seasons.

Norovirus (NoV) is one of the leading pathogens causing outbreaks of acute gastroenteritis (AGE). NoV is a single-stranded RNA virus with a highly diverse genome that can be classified into 10 genogroups (GI to GX). Among these, GI and GII are the most common genotypes causing AGE and are further divided into 9 GI and 27 GII genotypes based on amino acid sequences of the complete viral protein 1 (VP1), while 14 GI and 37 GII P types have been identified based on partial nucleotide sequences of the RNA-dependent RNA polymerase (RdRp) regions (*1*).

The GII.4 norovirus has been the predominant genotype in global epidemics, with novel pandemic GII.4 variants emerging approximately every 2–3 years since the mid-1990s, including GII.4 US95/96, Farmington Hills 2002, Hunter 2004, Den Haag 2006, New Orleans 2009, and Sydney 2012 (*2*). However, since 2014, novel non-GII.4 genotypes have emerged as the primary cause of outbreaks, surpassing GII.4 in China and other countries, including GII.17 in the winter season of 2014–2015 and GII.2[P16] in 2016–2017 (*3*–*5*).

Since February 2017, a significant increase in AGE outbreaks has been observed in a district of Beijing. To better understand the genetic variation of norovirus causing these recent acute gastroenteritis outbreaks, we analyzed the genetic characteristics of norovirus detected from AGE outbreaks during 2017–2024.

METHODS

Source of Specimens

Fecal specimens or anal swabs were collected from AGE cases in a district of Beijing from 2017 to 2024. AGE was defined as three or more episodes of diarrhea and/or two episodes of vomiting within 24 hours. A norovirus outbreak was defined as three or more AGE

cases occurring in the same location within three days, with at least two laboratory-confirmed NoV cases (*6*).

Genotyping and Sequence Analysis

NoV detection and genotyping were performed on positive samples using previously described protocols (*7*). Genotypes were determined using the Norovirus Typing Tool (http://www.rivm.nl/mpf/norovirus/typingtool). The complete RdRp and VP1 genomic fragments of GII.7[P7] (Supplementary Table S1, available at https://weekly.chinacdc.cn/) were amplified. Nucleotide sequence alignment was performed using MEGA v5.0. The optimal nucleotide substitution models for Bayesian evolutionary analysis of the GII.7 VP1 (1,623 bp) and RdRp (1,530 bp) coding genes were determined using PhyloSuite v1.2.2. Parameter settings were configured in BEAUti v1.10.4, and path sampling was employed to identify the best combination of molecular clock and population growth models. The reliability of posterior results was assessed using Tracer v1.7.2, with convergence considered achieved when all parameters had an ESS (Effective Sample Size) >200. The maximum clade credibility tree was constructed using TreeAnnotator v1.10.4, and phylogenetic tree visualization was enhanced using the Chiplot website. Validation in BEAST v1.10.4 confirmed that the strict molecular clock model and constant population growth model were applied for the evolutionary analysis of VP1 (HKY) and RdRp (GTR). Reference sequences for NoV were obtained from the GenBank database. The χ^2 test was used to compare differences among strains, with significance assumed at $P<0.05$. All statistical analyses were performed using IBM SPSS Statistics 25.0.

RESULTS

Epidemiological Distribution of NoV Outbreaks

Between January 2017 and June 2024, a total of 309 acute gastroenteritis outbreaks occurred in a district of Beijing, China, of which 150 (48.5%) were laboratory-confirmed as norovirus. GII was the predominant genogroup (125/150, 83.3%), followed by GI (23/150, 15.3%) and multiple genotypes (2/150, 1.3%). Two significant seasonal peaks were observed during March-April and November-December each year (Figure 1). Schools were the most frequent outbreak setting (145/150, 96.7%), including primary schools (68/145, 46.9%), kindergartens (61/145, 42.1%), middle schools (14/145, 9.6%), and universities (2/145, 1.4%). Person-to-person transmission was reported in 98.0% (147/150) of outbreaks, while foodborne transmission accounted for only 2.0% (3/150).

Genotype Distribution

Of 895 NoV-positive samples confirmed by real-time RT-PCR, 796 samples from 117 outbreaks were successfully genotyped by sequencing. Fifteen GI outbreaks were identified, comprising six genotypes: GI.6[P11] (4/15), GI.3[P13] (4/15), GI.5[P4] (3/15),

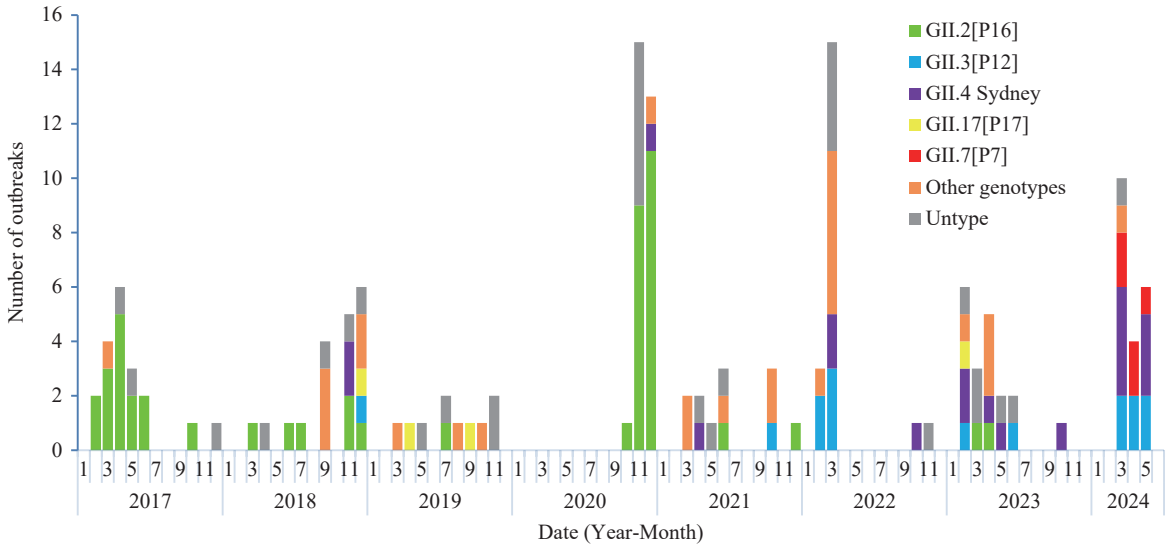

FIGURE 1. Genotype distribution of norovirus (NoV) outbreaks according to time from 2017 to 2024.

GI.4[P4] (2/15), GI.6[P6] (1/15), and GI.2[P2] (1/15). Among the 102 GII outbreaks, ten genotypes were identified, with non-GII.4 NoV outbreaks (83/102, 81.4%) significantly outnumbering GII.4 NoV outbreaks (19/102, 18.6%). The three most prevalent genotypes during the study period were GII.2[P16] (47/102, 46.1%), GII.3[P12] (15/102, 14.7%), and GII.4 Sydney[P16] (13/102, 12.7%). GII.2[P16] was the predominant genotype in 2017, 2018, and 2020, responsible for 100% (15/15), 54.5% (6/11), and 91.3% (21/23) of the GII outbreaks, respectively. GII.3[P12] was predominant in 2022 (5/9, 55.6%) and the second most prevalent genotype in the first half of 2024 (6/19, 31.6%). Among GII.4 Sydney variants, GII.4 Sydney[P16] was predominant only in the first half of 2024 (7/19, 36.8%), while GII.4 Sydney[P31] caused only 6 outbreaks throughout the entire study period. No clear predominant genotype was observed in 2019, 2021, and 2023. Notably, a novel GII.7[P7] strain was detected for the first time in March 2024, accounting for 26.3% (5/19) of GII outbreaks in Beijing during the first half of 2024 (Figure 1).

Among the GII genotyped outbreaks, GII.2[P16] was associated with the widest range of outbreak settings, primarily occurring in kindergartens and primary schools (87.2%, 41/47). In contrast, GII.3[P12] and GII.7[P7] were exclusively detected in kindergartens and primary schools. GII.17[P17] outbreaks were limited to primary and middle schools, while GII.4 Sydney affected kindergartens, primary schools, and middle schools (Table 1). Several other GII genotypes caused ≤5 outbreaks throughout the study period, including GIX.1[GII.P15] (*n*=1), GII.12[P16] (*n*=2), GII.17[P17] (*n*=4), GII.8[P8] (*n*=4), and GII.6[P7] (*n*=5).

Information on patient age was available for 796 patients from 117 genotyped outbreaks. The proportion of male patients was significantly higher than female patients, with gender distributions differing significantly among NoV strains (P<0.05) (Table 2). The median age of affected cases was 8 years. The proportion of patients ≤5 years of age was higher for GII.4 Sydney (69.0%) and GII.7[P7] (65.2%), while GII.2[P16] and GII.3[P12] had higher proportions in the 6–9 years group. GII.17[P17] was more likely to be observed in cases 10–18 years of age (65.7%). The age distributions differed significantly among NoV strains (P<0.05) (Table 2).

TABLE 1. Genotype distribution of norovirus (NoV) outbreaks from 2017 to 2024 according to setting.

Setting	No. outbreaks of norovirus					
	GII.2[P16]	GII.3[P12]	GII.4 Sydney	GII.7[P7]	GII.17[P17]	Other genotypes
Kindergartens	19	9	14	2	0	17
Primary schools	22	6	3	3	3	31
Middle schools	4	0	2	0	1	7
Universities	1	0	0	0	0	1
Other	1	0	0	0	0	4
Total	47	15	19	5	4	60

TABLE 2. Genotype distribution of norovirus (NoV) outbreaks from 2017 to 2024 according to age and sex.

Characteristics	Total	Patients linked to outbreaks of norovirus [*n* (%)]							
		GII.2[P16]	GII.3[P12]	GII.4 Sydney	GII.7[P7]	GII.17[P17]	Other genotypes	X^2	*P*
Sex								12.65	<0.05
Male	462 (58.0)	199 (52.4)	45 (69.2)	57 (67.9)	15 (65.2)	22 (62.8)	124 (59.1)		
Female	334 (42.0)	181 (47.6)	20 (30.8)	27 (32.1)	8 (34.8)	13 (37.1)	85 (40.9)		
Age (year)								200.85	<0.05
0–5	231 (29.0)	99 (26.1)	24 (36.9)	58 (69.0)	15 (65.2)	0	35 (16.7)		
6–9	264 (33.2)	140 (36.8)	29 (44.6)	18 (21.4)	4 (17.4)	10 (28.6)	63 (30.1)		
10–18	180 (22.6)	95 (25)	12 (18.5)	4 (4.8)	4 (17.4)	23 (65.7)	42 (20.1)		
>19	121 (15.2)	46 (12.1)	0	4 (4.8)	0	2 (5.7)	69 (33.1)		
Total	796 (100.0)	380 (100.0)	65 (100.0)	84 (100.0)	23 (100.0)	35 (100.0)	209 (100.0)		

The Genome Analysis of the Novel GII.7[P7]

We analyzed 7 full VP1 genome sequences from this study alongside reference sequences from GenBank to generate time-scaled evolutionary trees for both VP1 and RdRp regions. Four distinct clusters of GII.7 strains were identified: GII.7(1990–2003), GII.7(2004–2009), GII.7(2008–2017), and GII.7(2015–2024). The GII.7(2015–2024) cluster contained two subclusters (SC): SC1 comprised two strains from Paraguay (MW305562) and the United Kingdom (MH218661) from the 2015/16 season, while SC2 consisted of all seven GII.7[P7] strains from our study, together with a Russian-2024 strain (PQ100948) (Figure 2A). In the RdRp region, all GII.P7 RdRp sequences grouped within cluster IV, which contained three sublineages (a–c). All 7 GII.7[P7] strains from our study, along with the Russian-2024 strain, formed sublineage 2 and were closely related to strains from Paraguay and the United Kingdom (sublineage 1) (Figure 2B).

DISCUSSION

In 2017, our laboratory joined the national norovirus outbreak laboratory network (CaliciNet China) and became one of the network laboratories in China (*8*). This study identified two significant seasonal peaks of norovirus outbreaks occurring in March-April and November-December, consistent with previous reports that norovirus outbreaks in the northern hemisphere, including China, generally peak from November to March of the following year (*9*). Norovirus outbreaks in this study primarily affected kindergartens and primary schools, with children under 12 years of age emerging as the most susceptible population, similar to findings from other regions of China (*8*). In contrast, in Western countries such as the United States and Norway, norovirus outbreaks predominantly occur in long-term care facilities (LTCF) and among people aged ≥65 years (*10*). These inconsistencies may be attributed to significant differences in the sensitivity and coverage of regional surveillance systems across different countries.

Since 2012, GII.4 Sydney has been the predominant norovirus genotype worldwide (*3*), existing as two types: GII.4 Sydney[P31] and GII.4 Sydney[P16]. These two genotypes have consistently been the predominant strains in both outbreaks and sporadic cases of AGE in many countries. However, novel non-GII.4 genotypes have been increasingly documented, particularly GII.17[P17] in the winter season of 2014-2015 and GII.2[P16] in 2016–2017, causing increased NoV outbreaks in China and other countries (*3*–*5*). In this study, while GII.4 Sydney[P16] only showed a significant increase in the first half of 2024, 93.75% of norovirus outbreaks in 2017 were caused by GII.2[P16], peaking in April. This pattern was consistent with the general trend observed throughout Beijing (*6*). No norovirus outbreaks occurred from January to September 2020 due to the implementation of home-based online classes during the COVID-19 pandemic. Norovirus outbreaks increased sharply after November 2020, with GII.2[P16] remaining the predominant genotype, a finding also observed in national surveillance data (*9*). Ao et al. analyzed the transmission of GII.2[P16] norovirus during the winter of 2016–2017 in China and found that it originated in Guangdong in late 2016 before spreading northward in 2017 (*11*), subsequently becoming the dominant genotype in norovirus outbreaks across China from 2016 to 2020 (*9*). According to Jin et al., GII.3[P12] primarily affected children, while GII.17[P17] outbreaks tended to infect older children and adults in China (*8*). These findings revealed that the median age of susceptible individuals varied depending on the norovirus genotype. GII.3[P12] was the second most common genotype in our study, with most strains detected in children under 9 years of age from 2022 to 2024. Phylogenetic analysis shows the evolution of GII.3[P12] norovirus in chronological order, which may be attributed to antigenic drift of the GII.3 VP1 protein and intergenic recombination (*12*).

In this study, a non-GII.4 genotype, GII.7[P7], drew our attention as it became a predominant genotype (26.3%), causing norovirus outbreaks during the first half of 2024. GII.7[P7] formed an independent branch in the phylogenetic tree, indicating that the GII.7[P7] strain in this study represents a novel GII.7 variant. The majority of surveillance data has shown that the detection rate of GII.7 typically ranges from <1% to 7% (*13*). In our study, GII.7[P7] infections were predominantly observed in children under 5 years old. Previous data from Australian norovirus outbreak monitoring showed that the median age of GII.7[P7] patients was 39 years (range: 1–89 years). Recently, a metagenomic study conducted in nine infants (aged 2 weeks to 12 months) from Mexico found that three infants were infected by GII.7[P7] (*14*). These data suggest that GII.7[P7] affects individuals across a wide age range.

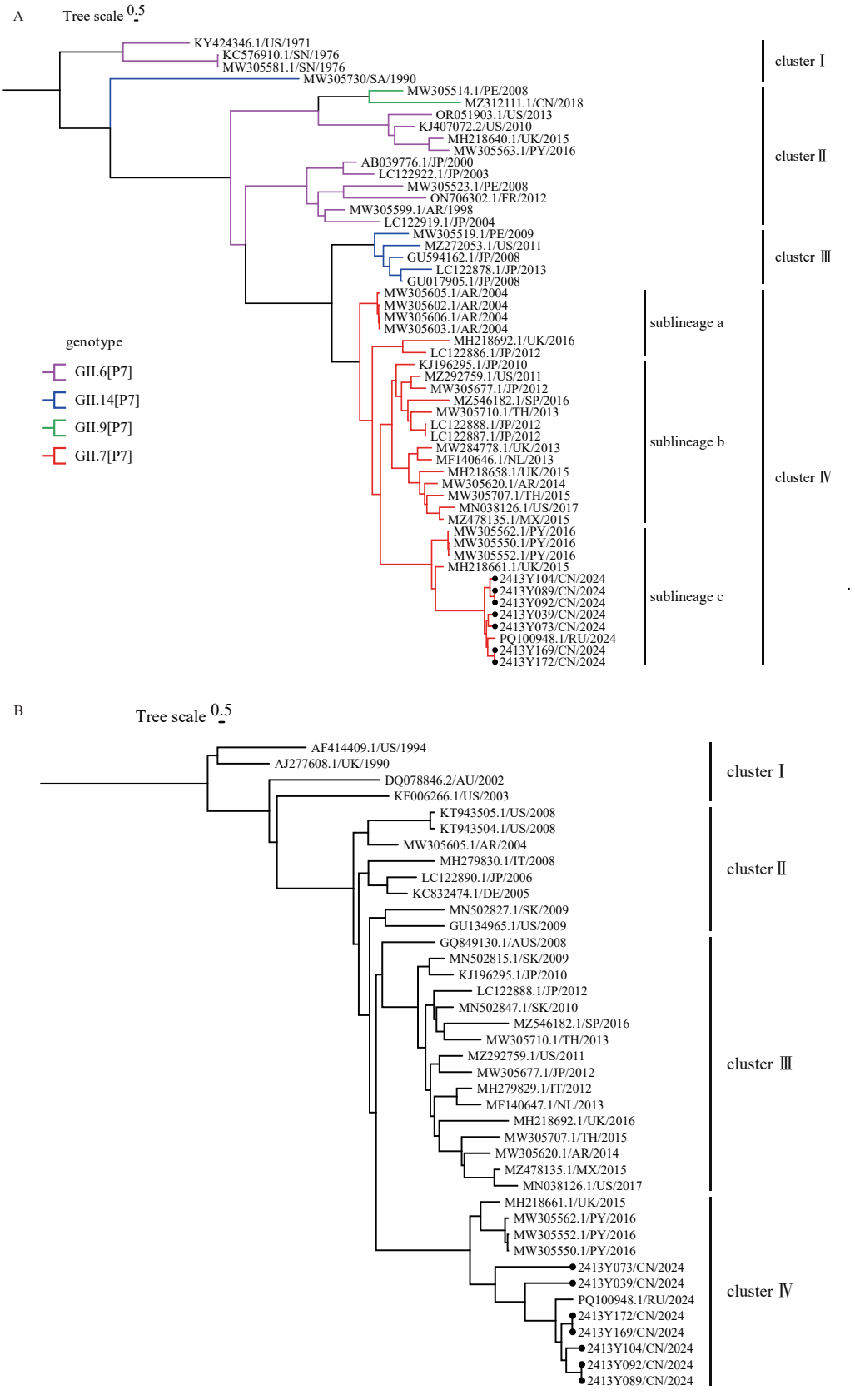

FIGURE 2. Phylogenetic analysis based on RdRp (1,530 bp) and VP1 (1,623 bp) gene of GII.7[P7]. (A) Phylogenetic tree for RdRp region; (B) Phylogenetic tree for GII VP1 region.
Note: Norovirus strains detected in this study were marked with the following symbols: ●.

In conclusion, we analyzed the epidemiological and genetic features of NoV outbreaks from January 2017 to June 2024 in Beijing. We observed significant changes in the predominant genotypes over time: GII.2[P16] was predominant in both 2017 and 2020, GII.3[P12] in 2022, multiple genotypes in 2023, and a novel GII.7[P7] variant in the first half of 2024. Further work to assess the spread of these genotypes and determine any differences in clinical severity or impact should be prioritized alongside molecular characterization as we approach the winter months.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Primers used for amplification of the complete genomic fragment of GII.7[P7] in this study.

Primers	Sequence (5'–3')	Size (bp)	Start Positions*
GII.7[P7]-ORF1_1-F	CTAACAAAGAAGAGGTTGGTG	1,296	49
GII.7[P7]-ORF1_1-R	GTGAAGATGATTTAGTGGACAG		1323
GII.7[P7]-ORF1_2-F	GTGTAAAGACCTAGGGAACTAC	1,154	1094
GII.7[P7]-ORF1_2-R	CACACTCATTGAATTTCACAT		2227
GII.7[P7]-ORF1_3-F	TGACAAAAATGGCAATACCC	1,200	1952
GII.7[P7]-ORF1_3-R	AACTCTCCAGACTTATGAACTTG		3129
GII.7[P7]-ORF1_4-F	GTCACTGGCTCAGACATCA	1,164	2877
GII.7[P7]-ORF1_4-R	AACAAGCTCATCTTTAAGCG		4021
GII.7[P7]-ORF1_5-F	AGGAAGCAAAGAAGACAGTG	1,141	3781
GII.7[P7]-ORF1_5-R	TTGATGACCATCTTGCTAACTTT		4899
GII.7[P7]-ORF2_1-F	GGCCTGATAAAACTGAAGGC	1,259	4541
GII.7[P7]-ORF2_1-R	TGCTGTGTACATCATTTCCAC		5779
GII.7[P7]-ORF2_2-F	AATTTCTTCCATTACAATCAGGG	1,164	5533
GII.7[P7]-ORF2_2-R	CCCCAGCATTTATGAGTGAA		6676
GII.7[P7]-ORF3-F	CCAACACTTCTATCAAGAAGC	1,031	6417
GII.7[P7]-ORF3-R	TCTTTTCACTAAATCTGTGACTCC		7424

* The start position in strain Arg4416 (accession No: MW305606).

Preplanned Studies

Prevalence of Micronutrient Deficiencies in Children and Adolescents Aged 3–17 Years — 14 PLADs, China, 2019–2021

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Summary

What is already known about this topic?

Micronutrient deficiencies in children represent a significant global health challenge. Currently, there are limited nationally representative reports on micronutrient deficiencies among Chinese children and adolescents.

What is added by this report?

This study presents nationally representative data on six micronutrient deficiencies. Among children and adolescents aged 3–17 years in China, the overall prevalence of vitamin A deficiency, marginal vitamin A deficiency, vitamin D deficiency, vitamin D insufficiency, iron deficiency, zinc deficiency, low selenium status, and copper deficiency were 0.3%, 12.1%, 23.9%, 41.2%, 10.9%, 3.3%, 7.1%, and 1.6%, respectively.

What are the implications for public health practice?

Among children and adolescents aged 3–17 years in China, vitamin D deficiency in adolescents (12–17 years), iron deficiency in adolescent girls (12–17 years), and low selenium status in rural areas emerge as the most prevalent micronutrient deficiencies requiring targeted interventions.

ABSTRACT

Introduction: Micronutrient deficiencies in children remains a significant global health challenge. This study presents the recent prevalence of micronutrient deficiencies among children and adolescents aged 3–17 years in China.

Methods: Using data from the National Nutrition and Health Systematic Survey for children aged 0–18 years in China (2019–2021), we analyzed the prevalence of six micronutrient deficiencies (vitamin A, vitamin D, iron, zinc, selenium, and copper) in children aged 3–17 years.

Results: A total of 9,121 children were included. The prevalence across age groups (3–5, 6–8, 9–11, 12–14, and 15–17 years) was 0.6%, 0.6%, 0.3%, 0.3%, and 0.1% for vitamin A deficiency; 18.8%, 22.2%, 13.9%, 7.8%, and 4.4% for marginal vitamin A deficiency; 4.5%, 9.8%, 17.6%, 36.3%, and 35.6% for vitamin D deficiency; 26.8%, 39.8%, 44.1%, 44.4%, and 40.9% for vitamin D insufficiency; 4.4%, 4.2%, 5.2%, 17.0%, and 18.3% for iron deficiency; 3.0%, 1.5%, 2.6%, 4.7%, and 4.4% for zinc deficiency; 5.7%, 5.7%, 7.7%, 9.0%, and 6.6% for low selenium status; and 1.1%, 1.6%, 1.9%, 1.2%, and 1.7% for copper deficiency, respectively.

Conclusions: Among children aged 3–17 years in China, vitamin D deficiency and iron deficiency emerge as the most prevalent micronutrient deficiencies.

Micronutrient deficiencies represent a significant public health concern among children aged 3–17 years, adversely affecting growth, immunity, and cognitive development. Despite the significance of this issue, comprehensive and current data on micronutrient deficiencies among Chinese children aged 3–17 years are limited. This study addresses this knowledge gap by characterizing the prevalence of vitamin A, vitamin D, iron, zinc, selenium, and copper deficiency in this age group using recent, nationally representative data from China.

This study was part of a cross-sectional National Nutrition and Health Systematic Survey for children aged 0–18 years conducted between 2019 and 2021 across 14 provincial-level administrative divisions (PLADs) in China. The project employed a multi-stage stratified randomized cluster sampling method, with

two PLADs randomly selected from each of the seven regions in China. One urban district and one rural county were randomly sampled from each PLAD, totaling 28 survey counties/districts. At each survey site, 132 children aged 3–5 years and 196 children aged 6–17 years were selected for each age group, with gender balance required throughout. Among the sampled children from each site, 10 children aged 3–5 years and 30 children aged 6–17 years were randomly cluster sampled from each age group for blood collection (*1*).

Morning fasting venous blood samples were collected from all participants. Serum retinol concentrations were measured using high-performance liquid chromatography (HPLC, Agilent Inc., USA). Serum $25(OH)D_2$ and $25(OH)D_3$ concentrations were determined via high-performance liquid chromatography-mass spectrometry (HPLC-MS, AB SCIEX, USA). Serum ferritin concentrations were measured using electrochemiluminescence immunoassay (cobas e 601, Roche Diagnostics, Mannheim, Germany). Plasma zinc and copper concentrations, along with whole-blood selenium levels, were analyzed using inductively coupled plasma mass spectrometry (ICP-MS, Agilent, 7700x, USA). Quality control samples for each micronutrient at both low and high concentrations were analyzed in each run. The inter-run coefficients of variation (CVs) for retinol, $25(OH)D_2$, $25(OH)D_3$, ferritin, zinc, selenium, and copper were 2.85%, 2.99%, 3.16%, 4.98%, 1.93%, 2.00%, and 1.78% for the low concentrations, and 2.90%, 2.90%, 2.91%, 5.84%, 1.63%, 2.52%, and 1.57% for the high concentrations, respectively. To control for inflammation-induced alterations in micronutrient concentrations, children with C-reactive protein (CRP) levels exceeding 5 mg/L were excluded from the analysis.

Vitamin A deficiency (VAD) and marginal vitamin A deficiency (mVAD) were defined by serum retinol concentration <0.2 mg/L and 0.2–0.3 mg/L, respectively (*2*). Vitamin D deficiency (VDD) and vitamin D insufficiency (VDI) were defined by serum 25(OH)D concentration <12 ng/mL and 12–20 ng/mL, respectively (*3*). Iron deficiency criteria were age-dependent: serum ferritin <12 μg/L for children under 5 years and <25 μg/L for children 5 years or older (*4*). Zinc deficiency was determined using age- and sex-specific thresholds: serum zinc <0.65 mg/L for children <10 years, <0.7 mg/L for girls ≥10 years, and <0.74 mg/L for boys ≥10 years (*5*). Low selenium status was defined as serum selenium <70 μg/L (*6*). Copper deficiency thresholds were age-stratified: serum copper <750 μg/L for children <10.3 years, <640 μg/L for children 10.3–12.5 years, and <570 μg/L for children >12.5 years (*7*).

Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA). Categorical variables were presented as percentages, and gender differences were compared using chi-squared tests. The prevalence of micronutrient deficiencies and their 95% confidence intervals (*CI*s) were calculated for defined age groups. Chi-squared tests were used to assess differences in deficiency prevalence across age groups, between genders within the same age and regional groups, and between urban and rural areas within the same age and gender strata. Statistical significance was set at $P<0.05$.

This study included 9,121 children aged 3–17 years, comprising 4,587 boys (50.3%) and 4,234 urban residents (46.4%). The age distribution was: 646 (7.1%) aged 3–5 years, 2,020 (22.1%) aged 6–8 years, 2,028 (22.2%) aged 9–11 years, 2,113 (23.2%) aged 12–14 years, and 2,314 (25.4%) aged 15–17 years (Table 1).

The overall prevalence of mVAD was 12.1% among children aged 3–17 years in China. mVAD prevalence was significantly higher in younger children aged 3–5 years (18.8%) and 6–8 years (22.2%) compared to those aged 9–11 years (13.9%), 12–14 years (7.8%), and 15–17 years (4.4%). While no significant difference was observed between the 3–5 and 6–8 years age groups ($P>0.05$), all other age group comparisons revealed statistically significant differences (all $P<0.05$). Among adolescents aged 15–17 years, girls in rural settings demonstrated significantly higher mVAD prevalence than boys ($P<0.05$). Additionally, mVAD prevalence was significantly higher in rural areas than in urban areas for children aged 6–11 years, regardless of gender (all $P<0.05$) (Table 2).

The overall prevalence of VDD among children aged 3–17 years in China was 23.9%. VDD prevalence was significantly higher in adolescents aged 12–14 years (36.3%) and 15–17 years (35.6%) compared to younger children aged 3–5 years (4.5%), 6–8 years (9.8%), and 9–11 years (17.6%). While no significant difference was observed between the 12–14 and 15–17 years age groups ($P>0.05$), all other age group

TABLE 1. Demographic characteristics of children aged 3–17 years by gender [*n* (%)].

Characteristics	Total (*n*=9,121)	Boys (*n*=4,587)	Girls (*n*=4,534)	χ^2	*P*
Region					
Urban	4,234 (46.4)	2,133 (46.5)	2,101 (46.3)	0.024	0.877
Rural	4,887 (53.6)	2,454 (53.5)	2,433 (53.7)		
Age group (years)					
3–5	646 (7.1)	329 (7.2)	317 (7.0)	0.849	0.932
6–8	2,020 (22.1)	1,028 (22.4)	992 (21.9)		
9–11	2,028 (22.2)	1,008 (22.0)	1,020 (22.5)		
12–14	2,113 (23.2)	1,054 (23.0)	1,059 (23.4)		
15–17	2,314 (25.4)	1,168 (25.5)	1,146 (25.3)		

comparisons revealed statistically significant differences (all $P<0.05$). Among children aged 6–17 years in urban areas and children aged 9–17 years in rural areas, girls exhibited significantly higher VDD prevalence than boys (all $P<0.05$). No significant urban-rural differences in VDD prevalence were observed across any age group regardless of gender (all $P>0.05$) (Table 2).

The overall VDI prevalence was 41.2% among children aged 3–17 years in China. VDI prevalence was higher in children aged 9–11 years (44.1%) and 12–14 years (44.4%) compared to those aged 3–5 years (26.8%), 6–8 years (39.8%), and 15–17 years (40.9%). No significant differences were found between the 9–11 and 12–14 years age groups ($P>0.05$), or between the 6–8 and 15–17 years age groups ($P>0.05$); however, all other age group comparisons revealed statistically significant differences (all $P<0.05$). In rural settings, girls demonstrated significantly higher VDI prevalence than boys ($P<0.05$) in the 6–8 years age group, while showing significantly lower VDI prevalence than boys ($P<0.05$) in the 12–14 years age group. VDI prevalence was significantly higher in urban areas than in rural areas for girls aged 12–17 years (all $P>0.05$) (Table 2).

Iron deficiency affected 10.9% of children aged 3–17 years in China, with significantly higher prevalence in adolescents aged 12–17 years compared to children aged 3–11 years (all $P<0.05$). Among adolescents aged 12–17 years, girls demonstrated significantly higher iron deficiency rates than boys in both urban and rural settings (all $P<0.05$). Among children aged 3–5 years, boys exhibited significantly higher iron deficiency rates than girls in rural areas ($P<0.05$). The prevalence of iron deficiency was higher in rural areas than in urban areas for boys aged 3–5 years ($P<0.05$). For girls aged 12–14 years, iron deficiency was more prevalent in urban areas, while for girls aged 15–17 years, it was more prevalent in rural areas (all $P<0.05$) (Table 2).

The prevalence of low selenium status among children aged 3–17 years in China was 7.1%. Children aged 9–14 years demonstrated significantly higher prevalence rates compared to those aged 3–8 years (all $P<0.05$). Among children aged 12–14 years in urban areas, the prevalence of low selenium status was significantly higher in boys than girls ($P<0.05$). A consistent pattern emerged, showing significantly higher prevalence rates in rural areas compared to urban areas across all age groups, regardless of gender (all $P<0.05$) (Table 2).

In this study, among children aged 3–17 years in China, the overall prevalence of VAD, zinc deficiency and copper deficiency were 0.3%, 3.3% and 1.6%, respectively.

DISCUSSION

This study provides current, nationally representative data on micronutrient deficiencies among children aged 3–17 years in China. Our findings highlight primary public health concerns requiring targeted interventions: vitamin D deficiency in adolescents (12–17 years), iron deficiency in adolescent girls (12–17 years), and low selenium status in rural areas.

Vitamin D deficiency and insufficiency remain a significant public health concern among children aged 3–17 years in China, with a particularly high deficiency prevalence in adolescents aged 12–17 years. Our results show that the prevalence of VDD and VDI in children aged 3–5 years (4.5% and 26.8%) has

TABLE 2. Prevalence of micronutrient deficiencies in children aged 3–17 years stratified by gender and region (%, 95% *CI*).

Characteristics		Age (years)	Vitamin A deficiency	Vitamin A marginal deficiency	Vitamin D deficiency	Vitamin D insufficiency	Iron deficiency	Zinc deficiency	Low selenium Status	Copper deficiency
Total		3–5	0.6 (0.2, 1.6)	18.8 (15.8, 22.1)*	4.5 (3.0, 6.5)*	26.8 (23.2, 30.6)*	4.4 (2.7, 6.8)*	3.0 (1.8, 4.7)*	5.7 (4.0, 7.8)*	1.1 (0.5, 2.3)
		6–8	0.6 (0.3, 1.0)	22.2 (20.4, 24.2)*	9.8 (8.5, 11.2)†	39.8 (37.6, 42.1)†	4.2 (3.4, 5.2)*	1.5 (1.0, 2.1)†	5.7 (4.7, 6.8)*	1.6 (1.1, 2.3)
		9–11	0.3 (0.1, 0.7)	13.9 (12.4, 15.5)†	17.6 (15.9, 19.4)§	44.1 (41.9, 46.4)§	5.2 (4.3, 6.3)*	2.6 (2.0, 3.5)†	7.7 (6.5, 9.0)†,§	1.9 (1.4, 2.7)
		12–14	0.3 (0.1, 0.7)	7.8 (6.5, 8.9)§	36.3 (34.1, 38.5)¶	44.4 (42.2, 46.7)§	17.0 (15.4, 18.7)†	4.7 (3.8, 5.7)*	9.0 (7.8, 10.4)†	1.2 (0.7, 1.7)
		15–17	0.1 (0, 0.3)	4.4 (3.6, 5.3)¶	35.6 (33.6, 37.7)¶	40.9 (38.9, 43.0)†	18.3 (16.6, 20.1)†	4.4 (3.6, 5.3)*	6.6 (5.6, 7.7)*,§	1.7 (0.1, 2.4)
Boys	Urban	3–5	0.6 (0, 3.5)	19.2 (13.4, 26.3)	1.4 (0.2, 4.9)	21.4 (15.0, 29.0)	2.1 (0.3, 7.5)††	3.7 (1.4, 7.8)	0.6 (0, 3.4)††	1.2 (0.2, 4.3)
		6–8	0.7 (0.2, 2.1)	16.5 (13.0, 20.4)††	6.4 (4.2, 9.2)**	37.9 (33.2, 42.9)	5.0 (3.2, 7.5)	1.7 (0.7, 3.5)	2.5 (1.2, 4.5)††	1.2 (0.4, 2.9)
		9–11	0.3 (0, 1.4)	11.0 (8.1, 14.5)††	10.3 (7.5, 13.7)**	44.4 (39.5, 49.6)	5.5 (3.5, 8.1)	2.4 (1.1, 4.4)	3.1 (1.6, 5.4)††	1.3 (0.4, 3.0)
		12–14	0.2 (0, 1.3)	7.5 (5.2, 10.4)	29.1 (24.8, 33.7)**	48.5 (43.6, 53.3)	8.7 (6.4, 11.6)**	0.7 (0.1, 2.0)**,††	3.9 (2.3, 6.2)**,††	1.1 (0.4, 2.6)
		15–17	0 (0, 0)	3.6 (2.3, 5.5)	29.0 (25.2, 32.9)**	41.9 (37.8, 46.1)	7.6 (5.3, 10.5)**	2.8 (1.6, 4.5)**	2.6 (1.5, 4.3)††	2.8 (1.6, 4.5)**
	Rural	3–5	1.9 (0.4, 5.4)	22.6 (16.4, 29.9)	4.8 (1.9, 9.6)	31.3 (23.9, 39.5)	8.3 (4.2, 14.3)**,††	2.5 (0.7, 6.3)	10.7 (6.4, 16.6)††	1.3 (0.2, 4.5)
		6–8	0.7 (0.2, 1.8)	26.3 (22.7, 30.1)††	8.0 (5.9, 10.6)	36.5 (32.5, 40.6)**	4.9 (3.2, 7.1)	1.1 (0.4, 2.5)	7.9 (5.8, 10.5)††	1.0 (0.3, 2.2)**
		9–11	0.4 (0, 1.3)	17.8 (14.7, 21.2)††	12.8 (10.1, 15.9)**	40.5 (36.4, 44.8)	4.0 (2.5, 6.0)	1.1 (0.4, 2.4)**	12.7 (10.0, 15.7)††	2.2 (1.2, 3.8)
		12–14	0.5 (0.1, 1.6)	10.1 (7.7, 13)	28.5 (24.7, 32.6)**	44.8 (40.6, 49.2)**	10.9 (8.4, 13.7)**	5.1 (3.4, 7.3)**,††	13.9 (11.1, 17.2)††	1.8 (0.9, 3.3)
		15–17	0.2 (0, 1.0)	2.1 (1.1, 3.6)**	26.8 (23.2, 30.7)**	40.9 (36.8, 45.1)	6.1 (4.2, 8.5)**	2.5 (1.4, 4.1)**	9.6 (7.3, 12.4)††	2.8 (1.6, 4.6)**
Girls	Urban	3–5	0 (0, 0)	16.7 (11.1, 23.6)	4.2 (1.6, 9.0)	22.5 (16.0, 30.3)	4.5 (1.2, 11.1)	4.5 (1.9, 9.1)	1.3 (0.2, 4.6)††	0.7 (0, 3.6)
		6–8	0 (0, 0)	14.9 (11.5, 18.8)††	13.5 (10.3, 17.4)**	43.0 (38.0, 48.1)	3.1 (1.6, 5.2)	2.4 (1.1, 4.5)	2.6 (1.3, 4.7)††	1.6 (0.6, 3.4)
		9–11	0.3 (0, 1.4)	9.6 (6.9, 12.9)††	23.9 (19.7, 28.4)**	47.7 (42.7, 52.8)	5.5 (3.5, 8.0)	4.4 (2.6, 6.9)	1.8 (0.7, 3.6)††	1.8 (0.7, 3.7)
		12–14	0.2 (0, 1.3)	5.7 (3.7, 8.2)	43.3 (38.5, 48.2)**	47.4 (42.5, 52.3)††	27.0 (23.1, 31.1)**,††	3.8 (2.3, 6.1)**,††	1.4 (0.5, 3.1)**,††	0.5 (0, 1.6)
		15–17	0 (0, 0)	5.3 (3.6, 7.5)	44.2 (39.9, 48.5)**	44.2 (39.9, 48.5)††	27.0 (22.8, 31.5)**,††	5.2 (3.5, 7.4)**	1.8 (0.9, 3.3)††	0.5 (0.1, 1.6)**
	Rural	3–5	0 (0.2, 1.9)	16.7 (11.2, 23.5)	7.6 (3.9, 13.2)	31.7 (24.3, 40.0)	2.2 (0.5, 6.4)**	1.3 (0.2, 4.6)	10.3 (6, 16.1)††	1.3 (0.2, 4.6)
		6–8	0.7 (0, 1.3)	27.7 (24.0, 31.7)††	11.4 (8.9, 14.5)	42.6 (38.4, 46.9)**	3.9 (2.4, 5.9)	1.0 (0.3, 2.2)	7.9 (5.8, 10.5)††	2.7 (1.5, 4.5)**
		9–11	0.4 (0, 1.0)	15.1 (12.2, 18.3)††	22.9 (19.5, 26.6)**	44.9 (40.7, 49.1)	6.1 (4.3, 8.5)	3.1 (1.8, 4.9)**	10.0 (7.6, 12.7)††	2.2 (1.1, 3.8)
		12–14	0.2 (0, 1.0)	7.0 (5.0, 9.4)	44.1 (39.9, 48.4)**	38.6 (34.5, 42.8)**,††	21.5 (18.2, 25.2)**,††	8.1 (5.9, 10.6)**,††	14.2 (11.3, 17.4)††	1.1 (0.4, 2.3)
		15–17	0.2 (0, 1.0)	6.6 (4.7, 9.0)**	43.1 (38.9, 47.4)**	36.8 (32.7, 41.0)††	33.1 (29.1, 37.3)**,††	7.2 (5.2, 9.7)**	12.5 (9.8, 15.6)††	0.7 (0.2, 1.8)**

Abbreviation: *CI*=confidence interval.

*, †, §, ¶ Values sharing the same superscript letter do not differ significantly ($P>0.05$), values with different superscript letters differ significantly ($P<0.05$) between age groups.

** Significant gender difference within the same age group and region ($P<0.05$).

†† Significant urban-rural difference within the same age group and gender ($P<0.05$).

improved compared with the prevalence reported in CNNHS 2010–2013 (8.9% and 43.0%) (*8*). However, the prevalence of VDD and VDI in children aged 6–17 years (25.3% and 42.3%) was similar to that reported in CNNHS 2015–2017 (18.6% and 43.3%) (*9*). The prevalence of VDD and VDI in our study population substantially exceeds that reported in NHANES 2017–2018 data (for children aged 5–11 years and 12–19 years, the prevalence of VDD was 1% and 7%, and the prevalence of VDI was 13% and 23%, respectively) (*10*).

Iron deficiency persists as a significant nutritional challenge, particularly among adolescent girls. The observed prevalence of iron deficiency in girls aged 12–17 years (27.1%) remains virtually unchanged from CNNHS 2015–2017 (27.6%) (*9*), indicating that current intervention strategies may be inadequate. This elevated prevalence likely stems from increased iron requirements during adolescence, primarily due to menstruation-associated iron losses. While NHANES 2011–2016 data showed that 15% to 22% of girls aged 12–18 years had serum ferritin levels below 15 μg/L (*11*), our findings indicate that the iron status among Chinese adolescent girls requires substantial improvement to reach levels comparable to their US counterparts.

Our findings demonstrate a substantial improvement in selenium status among rural Chinese children aged 6–17 years, with the prevalence of low selenium status (11.1%) showing marked reduction from historical levels of 43.8% in 2002 and 25.6% in 2012 (*12*). However, consistent with previous research (*13*), significant urban-rural disparities persist, with rural children continuing to exhibit a higher prevalence of low selenium status.

Addressing micronutrient deficiencies in children requires a multifaceted approach. For widespread deficiencies, food fortification or supplementation represents an effective intervention strategy. Encouraging increased meat consumption can help combat iron, zinc, and selenium deficiencies, while promoting outdoor activities can enhance vitamin D levels. A comprehensive combination of these strategies is crucial for effectively addressing nutrient inadequacies in children.

A major limitation of this study is the under-representation of children aged 3–5 years, who constituted only 7.1% (646 out of 9,121) of the study population. Additional research with enhanced representation of this age group is necessary to establish more generalizable findings.

In conclusion, vitamin D deficiency and iron deficiency were highly prevalent among Chinese children, particularly in school-aged children. Selenium status exhibited significant urban-rural disparities, with rural areas showing marked deficiency. Public health interventions should prioritize vitamin D and iron interventions for school-aged children, alongside targeted strategies to increase selenium levels in rural children.

Conflicts of interest: The authors declare no conflicts of interest.

Ethical statement: Approval from the Medical Ethical Review Committee at the National Institute for Nutrition and Health, Chinese Center for Disease Control and Prevention (No. 2019-009). Written informed consent was obtained from the guardians of all participating children.

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Preplanned Studies

HPV Genotypes and Associated Disease Prevalence in Males with Confirmed HPV Exposure — Shenzhen City, Guangdong Province, China, 2018–2022

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Summary

What is already known about this topic?

Human papillomavirus (HPV) is a globally prevalent sexually transmitted infection, with multiple genotypes strongly associated with cancers and other diseases. While extensive epidemiological data exist for HPV in females, studies on HPV genotype distribution in males, particularly those with confirmed HPV exposure, remain limited.

What is added by this report?

This study provides a comprehensive analysis of HPV genotype distribution and its association with clinical outcomes in males with confirmed HPV exposure. The results demonstrate that low-risk HPV genotypes predominate in this population, with certain diseases showing unique HPV genotype associations. Additionally, older males exhibited a greater tendency toward multiple genotype co-infections.

What are the implications for public health practice?

This study underscores the importance of including males in HPV vaccination programs. Expanding vaccination coverage to males, combined with early screening and targeted public health education, can effectively reduce HPV transmission between sexes and decrease the overall burden of HPV-related diseases.

ABSTRACT

Objectives: Human papillomavirus (HPV) is a globally prevalent infection, with multiple genotypes strongly associated with cancers and other diseases. While epidemiological studies in females are extensive, research on HPV genotype distribution in males remains limited.

Methods: We conducted a retrospective study by collecting and analyzing clinical and laboratory data from male patients with confirmed HPV infection at Shenzhen People's Hospital. The distribution of HPV genotypes and their associations with specific disease types were evaluated.

Results: A total of 2,037 male participants were included, with an overall HPV infection rate of 45%. Low-risk genotypes predominated, with HPV 6 and HPV 11 accounting for 25% and 12% of cases, respectively. High-risk genotypes such as HPV 16 and HPV 52 showed low prevalence (<3%) but exhibited a slight upward trend in 2022. No significant age distribution differences were observed between HPV-positive and HPV-negative groups. The frequency of multiple HPV genotype infections increased slightly with age. Specific HPV genotypes showed unique associations with acne (HPV 56), allergic dermatitis (HPV 59), and amyloidosis (HPV 58).

Conclusions: Low-risk HPV genotypes predominate in males with confirmed exposure. Older males appear more susceptible to multiple infections, and specific genotypes are associated with distinct diseases, supporting the need for male-targeted HPV vaccination and surveillance programs.

Human papillomavirus (HPV) is recognized as a leading cause of several diseases, including cervical cancer, anal cancer, penile cancer, oropharyngeal cancer, and genital warts (*1*–*6*). Despite significant advances in understanding HPV epidemiology in women, particularly with the widespread implementation of vaccination programs, the prevalence and clinical outcomes of HPV infection in men remain inadequately characterized (*7*).

HPV infection in men is associated with multiple conditions, including genital warts, anal dysplasia, and oropharyngeal cancer (*8*–*9*). However, comprehensive data on the distribution of different HPV genotypes in males, particularly those with confirmed HPV exposure, are limited. This study aims to address this knowledge gap by examining the prevalence of HPV

genotypes in a cohort of males with confirmed HPV exposure and investigating their relationship with clinical outcomes.

This study included 3,131 patients who underwent HPV detection at Shenzhen People's Hospital between September 18, 2018, and October 8, 2022. After excluding patients with incomplete information or unclear diagnoses, 2,037 patients were included in the final analysis. Diagnoses were confirmed by at least two experienced physicians, with the analyzed diseases including warts, amyloidosis, acne, folliculitis, allergic dermatitis, and others.

Patient samples were collected following comprehensive skin examinations of affected areas. Epidermal samples were obtained by scraping the upper epidermis using a scraper or scalpel, or by clipping small tissue pieces with biological tissue forceps. Skin slices were prepared by excising small sections from affected areas, while biopsies were performed using biological tissue forceps or scalpel under local anesthesia. DNA extraction was conducted using a Nucleic Acid Genotyping Kit for Human Papillomavirus (Flow Fluorescence Hybridization Method, Shanghai Tellgen), which detected 27 HPV genotypes, including 17 high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 26, 53, 82) and 10 low-risk types (6, 11, 40, 42, 43, 44, 55, 61, 81, 83) (https://www.tellgen.com/human_papillomavirus/HPV27_pro.htm). The DNA samples were homogenized by vortexing, followed by centrifugation and nucleic acid release, with the supernatant transferred for detection. PCR amplification followed a specific protocol involving initial denaturation, multiple amplification cycles, and final extension. Sequence alignment was performed using the blastn program (*10*).

This study investigated the prevalence of HPV infection in Shenzhen City, Guangdong Province, China, and analyzed demographic characteristics of participants. From a total of 3,131 male participants enrolled, all with female sexual partners who tested positive for HPV, 2,037 were included in the final analysis after data cleaning. The overall HPV infection rate was 45%. Analysis revealed no significant difference in age distribution between HPV-positive and HPV-negative groups, suggesting that age does not significantly influence HPV infection susceptibility (Figure 1).

The prevalence of HPV genotypes among males fluctuated throughout the study period (2018–2022). Negative cases increased from 47.99% in 2018 to 61.43% in 2020 before declining to 42.05% in 2022, while positive cases rose from 38.58% in 2020 to 57.95% in 2022. HPV 6 and HPV 11 were the most prevalent genotypes, reaching peaks of 12.92% and 6.82%, respectively. High-risk genotypes such as HPV 16 maintained low prevalence (<3%) but exhibited a slight upward trend in 2022 (Table 1).

Among HPV-positive participants, 27 distinct HPV genotypes were identified. Low-risk HPV genotypes showed significantly higher cumulative detection rates (47.77%) compared to high-risk types (25.63%) (Figure 2A). Similarly, the average detection rate of low-risk genotypes (3.18%) exceeded that of high-risk types (2.14%) (Figure 2B). Among low-risk types, the five most frequently detected genotypes were HPV 6 (25%), HPV 11 (12%), HPV 53 (6%), HPV 43 (6%), and HPV 59 (6%) (Figure 2C). For high-risk types, the most prevalent genotypes were HPV 52 (6%), HPV 16 (6%), HPV 51 (6%), HPV 39 (4%), and HPV 59 (3%) (Figure 2C). Further analysis clearly demonstrated the predominance of low-risk HPV

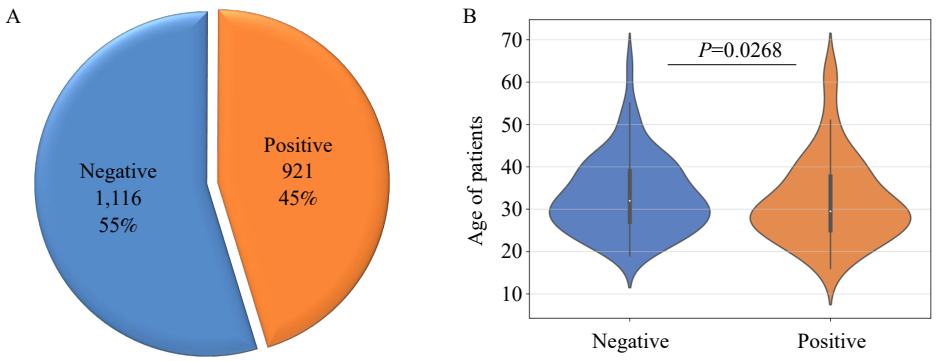

FIGURE 1. HPV infection status and age distribution of participants. (A) 45% of the participants showed positive HPV results. (B) There is no significant difference in age distribution between HPV-negative and HPV-positive participants.
Abbreviation: HPV=human papillomavirus.

TABLE 1. Annual distribution of HPV positivity and genotype prevalence in males.

Year	Negative (%)	Positive (%)	6 (%)	11 (%)	16 (%)	39 (%)	43 (%)	44 (%)	53 (%)	66 (%)	Other (%)
2018	47.99	52.01	11.07	4.36	3.02	1.34	1.01	0.34	0.00	2.01	31.87
2019	52.54	47.47	12.92	5.36	1.63	0.19	1.05	0.29	0.96	0.29	26.27
2020	61.43	38.58	11.18	4.90	1.51	0.13	0.63	0.25	0.25	0.00	21.99
2021	51.66	48.35	13.72	4.54	1.00	1.00	1.88	0.66	1.00	0.33	27.59
2022	42.05	57.95	7.95	6.82	1.14	2.27	2.27	3.41	2.27	1.14	29.95

Abbreviation: HPV=human papillomavirus.

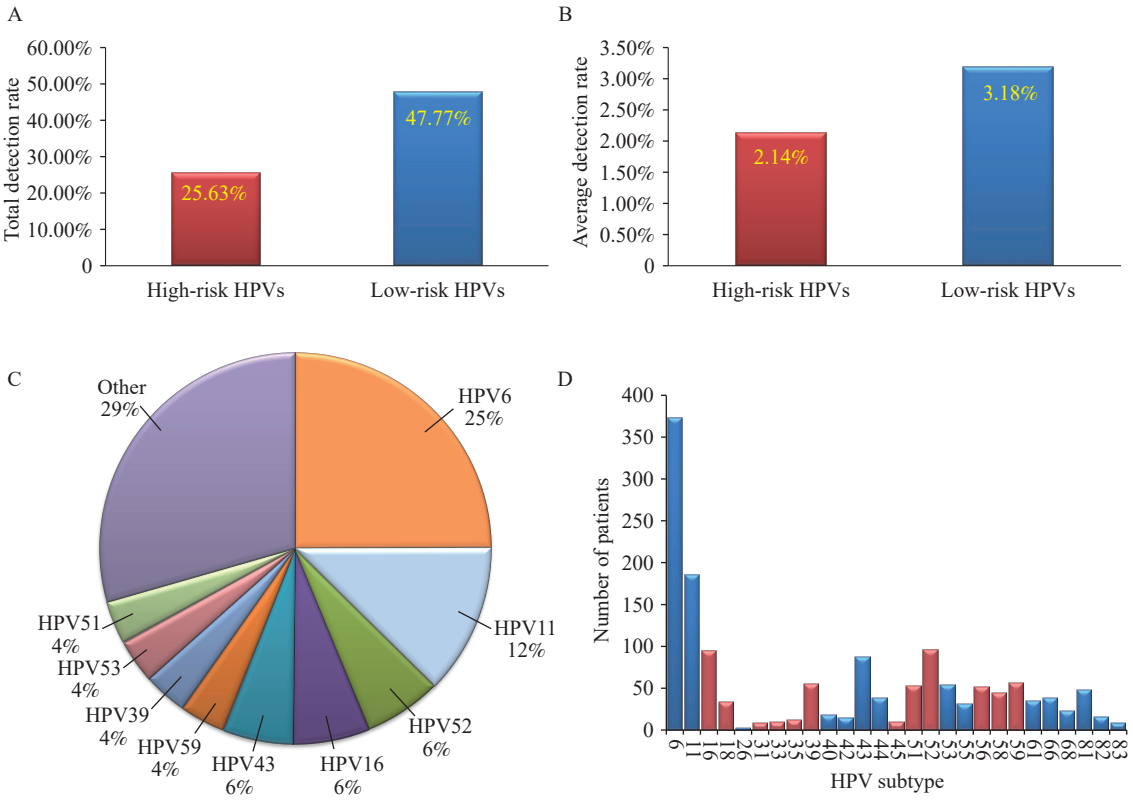

FIGURE 2. Detection rates and genotype distribution of high-risk and low-risk HPV genotypes. (A) Total detection rate of high-risk and low-risk HPV genotypes. (B) Average detection rate of high-risk and low-risk HPV genotypes. (C) Proportion of each HPV genotype among HPV-positive participants. (D) Distribution of high-risk and low-risk HPV genotypes among positive participants.
Note: For (D), The histograms show the distribution of high-risk (blue) and low-risk (red) HPV genotypes among positive participants.
Abbreviation: HPV=human papillomavirus.

genotypes among positive participants (Figure 2D).

Significant variations were observed in the distribution of high-risk HPV genotypes among the male population. HPV 16 and HPV 52 exhibited the highest prevalence (18% each), followed by HPV 39 and HPV 59 (11% each), while other genotypes including HPV 18, 51, and 56 showed relatively lower prevalence (Figure 3A). Age distribution analysis revealed that HPV 16 and HPV 18 infections were more common in younger individuals, whereas HPV 52, 59, and 39 were detected across a broader age range, including older individuals, suggesting genotype-specific age patterns (Figure 3B). Further analysis of the relationship between age and multiple genotype infections revealed a gradual increase in the number of genotypes detected with increasing age, indicating a weak positive correlation and suggesting that older males may be more susceptible to multiple HPV genotype co-infections (Figure 3C).

This study explored the relationship between HPV genotypes and various skin and genital diseases. Patients with warts exhibited diverse HPV genotype

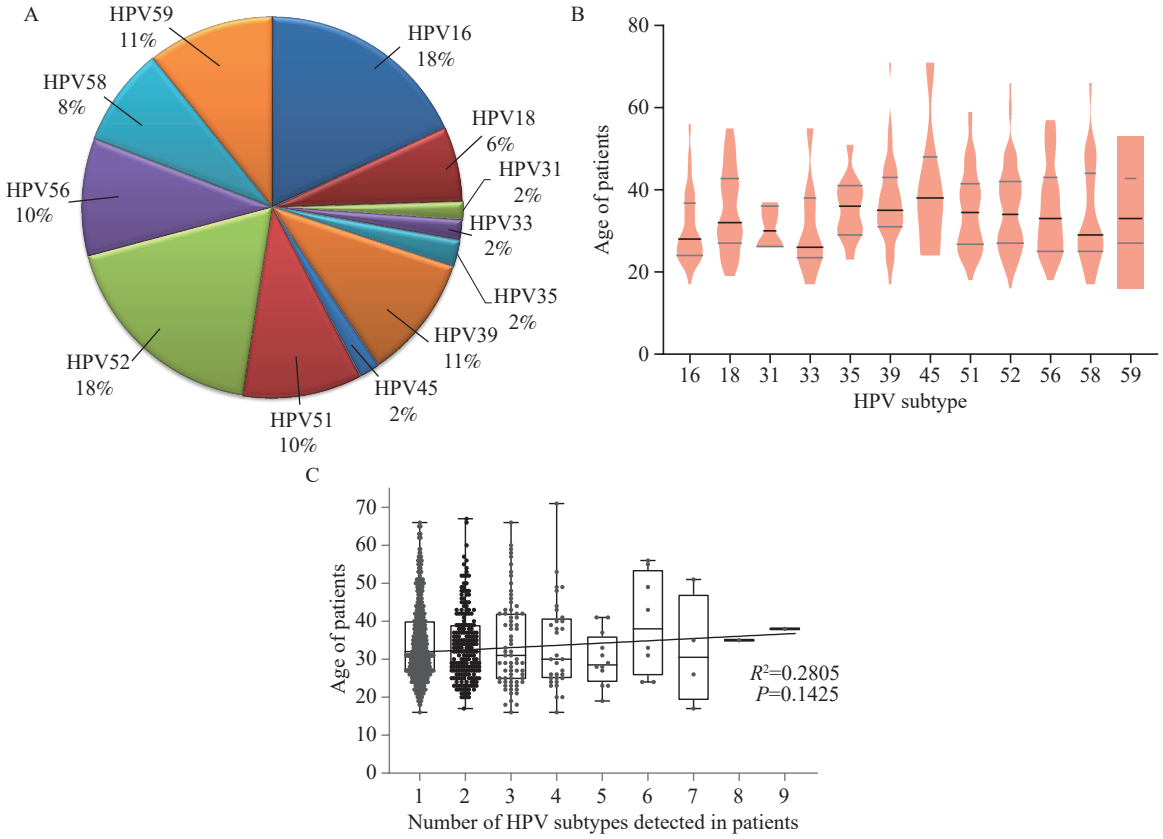

FIGURE 3. Distribution of high-risk HPV genotypes and their association with patient age. (A) Proportion of high-risk HPV genotypes. (B) Age distribution of participants infected with different high-risk HPV genotypes. (C) Relationship between multiple HPV genotypes and age in HPV-positive participants.
Abbreviation: HPV=human papillomavirus.

infections with no predominant type. In folliculitis patients, HPV 6 and HPV 52 were the most common genotypes detected. Notably, specific HPV genotypes showed unique associations with certain conditions: HPV 56 with acne, HPV 59 with allergic dermatitis, and HPV 58 with amyloidosis. Among balanitis patients, HPV 58 was most prevalent (39.29%), followed by HPV 55 and HPV 59 (17.86% each). Warts patients demonstrated the most diverse HPV genotype profile, with HPV 6 being the most frequently detected, while other genotypes occurred at lower frequencies. In patients with urethritis, HPV 6, HPV 53, and HPV 52 were the predominant genotypes (Figure 4).

DISCUSSION

This study investigated the prevalence of HPV infection among males in Shenzhen City, Guangdong Province, China, revealing an overall infection rate of 45%. Notably, no significant age-related differences were observed between HPV-positive and HPV-negative groups, suggesting that age has minimal influence on HPV infection susceptibility in this population.

The genotype distribution analysis demonstrated a clear predominance of low-risk HPV types, with HPV 6 and HPV 11 accounting for 25% and 12% of positive cases, respectively. High-risk genotypes, particularly HPV 16, exhibited relatively low prevalence (<3%) but showed a concerning upward trend in recent years. The overall HPV positivity rate fluctuated throughout the study period, with negative cases increasing from 2018 to 2020, followed by a substantial rise in positive cases in 2022.

Our age-stratified analysis revealed a modest positive correlation between age and the number of HPV genotypes detected, indicating that older individuals may be more susceptible to multiple genotype co-infections. Specific genotype-age associations were also observed, with HPV 16 and HPV 33 more frequently detected in younger participants, while HPV 35 and HPV 45 showed higher prevalence among older individuals.

FIGURE 4. HPV genotypes in patients with (A) warts; (B) folliculitis; (C) acne; (D) allergic dermatitis; (E) amyloidosis.
Abbreviation: HPV=human papillomavirus.

The study also identified distinct associations between specific HPV genotypes and various dermatological and genital conditions. Patients with warts demonstrated the most diverse HPV genotype profile, while certain conditions showed exclusive associations with specific genotypes — acne with HPV 56, allergic dermatitis with HPV 59, and amyloidosis with HPV 58. These findings suggest potential genotype-specific pathogenic mechanisms that warrant further investigation.

This study has several limitations that should be considered when interpreting the results. First, it was conducted exclusively in Shenzhen City, Guangdong Province, China, which may limit the generalizability of findings to other regions or populations with different demographic characteristics or health conditions. Future research should encompass broader geographic areas to validate these findings. Second, the use of a hospital-based cohort may introduce selection bias. A multicenter approach would enhance sample representativeness and improve the generalizability of results.

The findings of this study have significant implications for public health strategies, particularly for

improving HPV vaccination programs. Currently, vaccination efforts predominantly target females, overlooking males as essential vectors in HPV transmission (*11*). This gender-specific approach fails to effectively address HPV across the entire population. Expanding vaccination programs to include males represents a critical opportunity to address this gap. Educational campaigns should raise awareness among males about HPV infection risks and vaccine effectiveness. Emphasizing prevention, early intervention, and male inclusion in vaccination programs can substantially reduce the overall burden of HPV-related diseases and improve global public health outcomes.

In conclusion, this study highlights the high prevalence of HPV infection among males with confirmed exposure and identifies significant associations between specific HPV genotypes and certain diseases. Implementing targeted prevention and intervention strategies for males, including vaccination and early screening, not only benefits male health but also plays a crucial role in controlling HPV transmission. This comprehensive approach ultimately contributes to female health protection and reduces the overall public health burden of HPV-related diseases.

Conflicts of interest: No conflicts of interest.

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Outbreak Reports

A Foodborne Disease Outbreak Caused by *Salmonella* — Guiyang City, Guizhou Province, China, September 2024

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Summary

What is already known about this topic?

Salmonella infection represents a common etiology of foodborne disease outbreaks in educational settings, posing substantial health risks to both students and faculty while simultaneously generating significant public concern. This constitutes a major public health challenge requiring vigilant surveillance and intervention.

What is added by this report?

On September 11, 2024, the local center for disease control and prevention received notification from a school physician regarding a clustered foodborne disease outbreak at a middle school. Investigators promptly deployed to assess the situation. Based on comprehensive epidemiological investigations, environmental hygiene assessments, clinical symptomatology, and laboratory analyses, the outbreak was determined to be caused by *Salmonella* contamination. Specifically, *Salmonella* Newport was detected in 22 patients, 1 canteen worker, and 3 food samples.

What are the implications for public health practice?

We have implemented measures to identify the pathogenic agent, contaminated food vehicles, and associated risk factors, while emphasizing preventive and control recommendations to mitigate similar incidents in the future. The risk of foodborne illness caused by *Salmonella* Newport contamination warrants serious consideration, and public health practitioners must maintain heightened vigilance against this pathogen.

ABSTRACT

Introduction: On September 11, 2024, a foodborne disease outbreak occurred at a middle school. Upon receiving the report, investigators promptly arrived at the scene to verify the incident, identify suspicious food items and risk factors that contributed to the outbreak, providing a reference for the prevention and investigation of similar incidents in the future.

Methods: Epidemiological methods were employed to characterize the clinical and epidemiological features of cases. A case-control study was conducted to identify suspicious meals and food items. Samples from cases, food products, and environmental sources were collected for laboratory testing.

Results: A total of 112 cases met the case definition, with an attack rate of 3.20%. The predominant clinical manifestations included fever (100.00%), diarrhea (92.86%), and vomiting (34.82%). The case-control study indicated that egg cakes and soybean milk sold at window 17 of the Second canteen were the suspicious food items. By September 12, 252 samples had been collected, with laboratory testing detecting *Salmonella* Newport in 26 samples.

Conclusion: Based on epidemiological investigation, hygienic assessment, and laboratory testing results, this incident is classified as an outbreak of foodborne disease caused by *Salmonella* Newport contamination. The health and well-being of students is paramount, necessitating strengthened food hygiene supervision in schools, regular food safety knowledge training, and comprehensive measures to reduce the risk of foodborne disease in educational settings.

At 12:50 p.m., September 11, 2024, the local CDC received a report from a school doctor regarding multiple students exhibiting symptoms including vomiting, diarrhea, and fever. Investigators promptly arrived at both the hospital where cases were concentrated and the school where the incident occurred to verify the situation. During the investigation, additional students continuously presented at the hospital emergency department with symptoms of fever, diarrhea, and vomiting. They immediately activated the provincial response

mechanism and established a coordinated provincial, municipal, and county-level investigation team to conduct a comprehensive epidemiological investigation.

This investigation aimed to confirm the cause of the clustering event, identify potential risk factors, and implement effective preventive and control measures.

INVESTIGATION AND RESULTS

The school encompasses an area of 678 hectares with a total built area of 18,000 square meters. It accommodates 3,193 students and 312 teachers (1,472 in middle school and 1,721 in high school). The institution operates 2 dining facilities, designated as the First and Second canteens, which provide 3 daily meals: breakfast, lunch, and dinner. The First canteen employs 69 food service workers, while the Second canteen has 48 staff members. Beginning at 07:00 on September 10, students and teachers across multiple classes began experiencing symptoms including diarrhea, abdominal pain, vomiting, and fever. Case numbers peaked on September 11, as illustrated in Figure 1.

Case identification was conducted through multiple channels, including review of case information from local medical institutions, the National Foodborne Disease Case Surveillance Network, examination of school illness-related absence records, and interviews with affected students and their families. Since September 8, 2024, it identified individuals who experienced fever (≥37.5 ℃) and diarrhea (≥3 times/24 hours) or vomiting (with expulsion of gastric contents ≥1 time), with or without accompanying symptoms such as headache, nausea, abdominal pain, or dizziness after consuming meals at the school. Among 3,505 individuals investigated, 112 met the case definition, yielding an attack rate of 3.20%.

Among the 112 cases, 46 were 12-year-old students, 59 were students aged 13–16 years, with the age range spanning from 12 to 53 years. The affected population included 3 teachers and 1 canteen worker. The male-to-female ratio was 1.15∶1, comprising 60 males and 52 females. Clinical manifestations predominantly included fever in all 112 cases (100.0%), diarrhea in 104 cases (92.86%), and vomiting in 39 cases (34.82%), with predominantly watery stool consistency, often accompanied by additional symptoms such as headache, dizziness, limb weakness, and nausea. By September 13, all patients had stabilized with no severe cases and significant symptomatic improvement. As depicted in the epidemic curve (Figure 1), case distribution included 17 cases on September 10, 82 cases on September 11, and 6 cases on September 12. The temporal distribution of case onset was concentrated between 00:00 and 23:00 on September 11.

To further identify the suspicious food items implicated in this outbreak, it conducted a case-control study comparing 112 cases (including both suspected and confirmed cases) with 221 controls who dined at the same locations during the same time period since September 8, 2024, but remained asymptomatic. Based on the epidemic curve and typical incubation period, we hypothesized that the contaminated food was consumed on September 10. Our investigation revealed that most affected individuals had dined in the Second canteen. Analysis of meals served in this canteen on September 10 showed statistically significant associations for breakfast [odds ratio

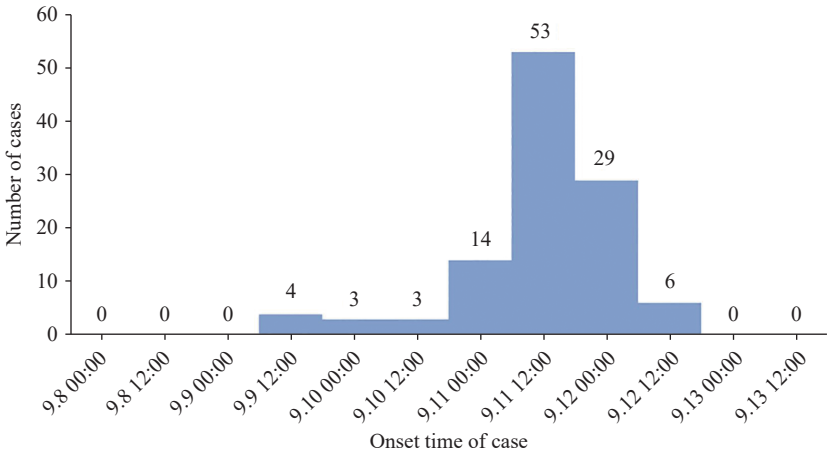

FIGURE 1. Epidemic curve of a *Salmonella* contamination in a middle school (*n*=112).

(*OR*)=7.026; 95% confidence interval (*CI*): 4.228, 11.674], lunch (*OR*=6.896; 95% *CI*: 4.120, 11.540), and dinner (*OR*=7.845; 95% *CI:* 4.584, 13.427), as shown in Table 1. To control for potential confounding factors, this study performed logistic regression analysis on all three meals served on September 10. The results indicated that breakfast was not statistically significant after adjustment. The adjusted *OR*s are presented in Table 1. Based on this preliminary analysis, lunch and dinner served at the Second canteen were identified as the suspicious meals. A detailed analysis was subsequently conducted for all serving windows providing lunch and dinner in the Second canteen on September 10. Window 17 primarily served noodle products, Window 18 served rice, and Window 19 sold pre-packaged foods such as milk and mineral water. Our analysis revealed that both lunch (*OR*=21.500; 95% *CI*: 8.768, 52.718) and dinner (*OR*=7.852; 95% *CI*: 3.555, 17.342) from Window 17 were statistically significant, identifying Window 17 as the suspicious serving location, as shown in Table 2. Further analysis of specific food items served at Window 17 for lunch and dinner on September 10 demonstrated that soybean milk (*OR*=3.351; 95% *CI*: 2.829, 3.969) and egg cakes *(OR*=3.085; 95% *CI*: 2.638, 3.608) at lunch, as well as soybean milk (*OR*=3.278; 95% *CI*: 2.777, 3.870) and egg cakes (*OR*=6.350; 95% *CI*: 1.684, 23.948) at dinner, were all statistically significant risk factors, as shown in Table 3. To strengthen our analysis, this study stratified cases based on consumption patterns: those who consumed only egg cakes, only soybean milk, or both items, as detailed in the Supplementary Table S1(available at https://weekly.chinacdc.cn/). The results consistently identified both egg cakes and soybean milk as significant risk factors. Therefore, our epidemiological investigation strongly implicated egg cakes and soybean milk served at Window 17 of the Second canteen on September 10 as the likely contaminated food vehicles, warranting further laboratory confirmation.

The school campus serves approximately 3,300 individuals daily through two canteens, both operating with valid food business licenses and staffed by workers with current health certificates. The Second canteen can accommodate approximately 1,000 diners simultaneously per meal. It comprises three floors, with the upper levels designated as dining areas. The basement level, characterized by poor ventilation and proximity to the parking lot, functions as the food

TABLE 1. Case-control analysis of suspicious meals in a middle school.

Suspicious meal	Case		Non-case		*OR* (95% *CI*)	χ^2	Wald χ^2	*P*
	Exposed	Non-exposed	Exposed	Non-exposed				
Breakfast on Sep 10	80	32	58	163	7.026 (4.228, 11.674)	62.534	–	<0.001
Lunch on Sep 10	84	28	67	154	6.896 (4.120, 11.540)	59.882	–	<0.001
Dinner on Sep 10	89	23	73	148	7.845 (4.584, 13.427)	64.149	–	<0.001
Breakfast on Sep 10*	80	32	58	163	–	–	–	>0.05
Lunch on Sep 10*	84	28	67	154	47.300† (17.230, 129.846)	–	56.025	<0.001
Dinner on Sep 10*	89	23	73	148	19.304† (8.336, 44.705)	–	47.740	<0.001

Note: "–" means not applicable.
Abbreviation: *OR*=odds ratio; a*OR*=adjusted odds ratio; *CI*=confidence interval.
* Logistic regression analysis of suspicious meals in a middle school.
† a*OR*s.

TABLE 2. Case-control analysis of suspicious window in a middle school.

Suspicious window	Case		Non-case		*OR* (95% *CI*)	χ^2	*P*
	Exposed	Non-exposed	Exposed	Non-exposed			
Window 17 of lunch on Sep 10	42	70	6	215	21.500 (8.768, 52.718)	72.904	<0.001
Window 18 of lunch on Sep 10	1	111	0	221	2.991 (2.570, 3.481)	–*	>0.05
Window 17 of dinner on Sep 10	28	84	9	212	7.852 (3.555, 17.342)	32.961	<0.001
Window 18 of dinner on Sep 10	4	108	5	216	1.600 (0.421, 6.08)	–*	>0.05

Note: "–" means not applicable.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval.
* Fisher's exact test was used because the expected count was <5.

TABLE 3. Case-control analysis of suspicious food in a middle school.

Suspicious food	Case		Non-case		*OR* (95% *CI*)	χ^2	*P*
	Exposed	Non-exposed	Exposed	Non-exposed			
Soybean milk of lunch	18	94	0	221	3.351 (2.829, 3.969)	37.547	<0.001
Egg cake of lunch	6	106	0	221	3.085 (2.638, 3.608)	–*	<0.05
Soybean milk of dinner	15	97	0	221	3.278 (2.777, 3.870)	30.994	<0.001
Egg cake of dinner	9	103	3	218	6.350 (1.684, 23.948)	–*	<0.05

Note: "–" means not applicable.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval.
* Because the expected count was <5, Fisher's exact test was used.

processing and production area. The canteen layout is illustrated in the Supplementary Figure S1 (available athttps://weekly.chinacdc.cn/). During our on-site inspection, we observed inadequate cleaning of the pancake pan in the pastry processing area. Review of security camera footage revealed that workers did not wear gloves during egg cake preparation. Additionally, some Second canteen staff failed to properly wear masks and gloves during food service. The preparation processes for egg cakes and soybean milk are detailed in the Supplementary Figure S2 (available at https://weekly.chinacdc.cn/). The Second canteen's processing area exhibited multiple deficiencies, including inadequate separation of raw and cooked foods, absence of cleaning and disinfection records, and non-standardized food sample retention practices. These conditions created a substantial risk of cross-contamination between food processing equipment and prepared foods.

From 19:00 on September 11 to 13:00 on September 12, we collected a total of 252 samples from the investigation site. These included 145 human samples (144 anal swabs and 1 vomit sample), 59 environmental samples, 10 water samples, and 38 food samples. Preliminary polymerase chain reaction (PCR) screening indicated that 11 samples from patients and canteen workers tested positive for *Salmonella*. Among the 3 retained food samples from lunch and dinner served at the Second canteen on September 10, egg cake samples tested positive for *Salmonella*. Following bacterial culture and identification, a total of 26 samples were confirmed as *Salmonella* Newport (*S.* Newport), including 22 patient samples, 1 canteen worker sample, and 3 food samples (retained egg cake samples from September 10 and retained soybean milk samples from September 11).

DISCUSSION

Based on a comprehensive analysis of the epidemiological and hygienic investigation findings, clinical symptomatology, and laboratory test results, in conjunction with the "Diagnostic Criteria and Treatment Principles of *Salmonella* Food Poisoning" (WS/T 13-1996), it was determined that this incident constituted a cluster infection caused by *Salmonella* contamination of egg cakes and soybean milk sold at window 17 of the Second canteen. This conclusion is supported by several key findings: 1) Patients presented with consistent clinical manifestations — predominantly fever, diarrhea, abdominal pain, and vomiting — with a concentrated incubation period characteristic of *Salmonella* infection. 2) Hygiene investigation revealed significant irregularities in food sample retention practices and evidence of potential cross-contamination between processing tools and food items during preparation. Notably, canteen workers failed to wear gloves during egg cake production, and the same personnel who transported egg cakes to the sales window also prepared soybean milk. 3) Multiple PCR analyses confirmed *Salmonella* positivity in 11 clinical specimens and canteen worker sample, and 3 food samples. Subsequent bacterial culture identified *Salmonella* Newport in 26 samples. Although epidemiological analysis strongly implicated soybean milk, definitive evidence was limited by the absence of *Salmonella* detection in the retained soybean milk samples from September 10. This discrepancy may be attributed to cross-contamination during the sales process, whereby workers potentially contaminated by egg cakes subsequently prepared soybean milk. Additionally, the soybean milk collected by investigators had been stored in a sample cabinet after morning preparation, suggesting it may not have been contaminated at the time of collection.

Salmonella represents a prevalent foodborne pathogen, with numerous emerging strains demonstrating enhanced virulence and antimicrobial resistance (*1*). Among these, *S.* Newport constitutes a particularly significant serotype (*2*). *S.* Newport

exhibits high detection rates in farmed animals, livestock carcasses, and animal-derived products including meat, eggs, and milk (*3*–*4*). Despite its prevalence in food sources, food poisoning outbreaks attributed specifically to *S*. Newport remain relatively uncommon in the literature. Previous investigations have documented *S*. Newport isolation from beef, duck meat, clinical specimens, and food handlers (*5*–*7*). In the present outbreak, *S*. Newport was detected in egg cake samples, patient specimens, and a canteen worker. The contamination pathway may have involved either the use of contaminated eggs in cake preparation, with subsequent transmission to ungloved workers during handling, or alternatively, asymptomatic carriage of the pathogen by food handlers who subsequently contaminated egg cakes during processing. Communication with Window 17 personnel revealed that soybean milk was freshly prepared for morning, afternoon, and evening service; however, unsold product was not promptly refrigerated but rather continued to be served at subsequent meals. Furthermore, the workers responsible for soybean milk production also transported egg cakes to the sales window, creating opportunities for cross-contamination. The subsequent distribution of contaminated products to students likely facilitated pathogen dissemination. Given the relative rarity of S. Newport food poisoning outbreaks, this pathogen warrants heightened vigilance and further epidemiological investigation.

This investigation employed a case-control methodology to identify exposure timing and implicated food vehicles, complemented by laboratory analyses for pathogen identification. However, several limitations merit acknowledgment. Practical constraints prevented identification of the index case, and comprehensive dietary histories were unavailable for approximately one-quarter of the population, potentially introducing bias into the case-control analysis. Additionally, genomic characterization of bacterial and food isolates was not performed, resulting in incomplete molecular epidemiological evidence. To prevent similar incidents, implementation of enhanced food hygiene supervision in educational institutions is imperative, including regular food safety training, standardization of food processing protocols, and prevention of cross-contamination throughout the food production, processing, storage, transportation, and service continuum. Prior to academic term commencement, a combination of mandatory and random inspections should be instituted to evaluate preparedness, with rigorous assessment of equipment functionality, food supply chains, and environmental conditions to identify and mitigate potential safety hazards.

Conflicts of interest: No conflicts of interest.

Ethical statement: Granted by Ethics Committee of Guizhou Provincial Center for Disease Control and Prevention (Q2024-07).

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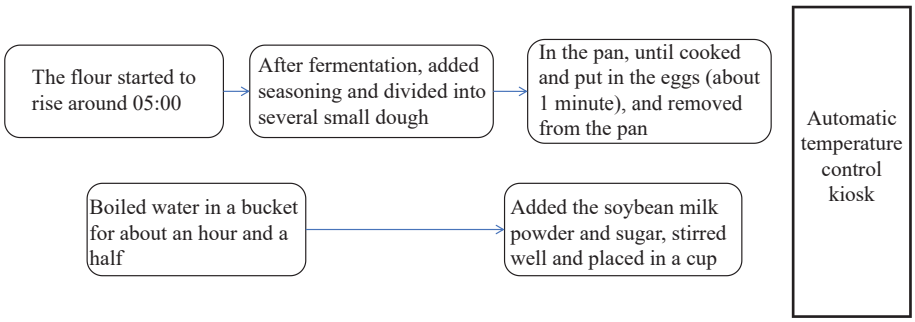
SUPPLEMENTARY MATERIAL

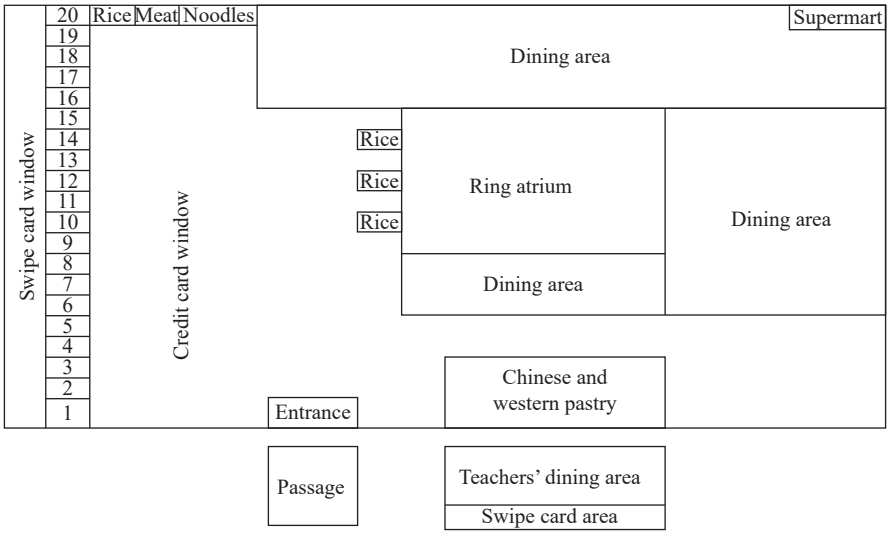
SUPPLEMENTARY TABLE S1. The consumption patterns of egg cake and soybean milk among cases on September 10.

	Soybean milk of lunch*	Egg cake of lunch†	Soybean milk and egg cake of lunch§	Soybean milk of dinner*	Egg cake of dinner†	Soybean milk and egg cake of dinner§
Case	18	6	4	15	9	7
Non-case	0	0	0	0	3	0

* Consumption of soybean milk only.
† Consumption of egg cake only.
§ Consumption of both soybean milk and egg cake.



SUPPLEMENTARY FIGURE S1. Process flow chart for egg cake and soybean milk production.



SUPPLEMENTARY FIGURE S2. Layout map of the Second canteen in a middle school.

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