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Global trends in adult viral gastroenteritis: A comprehensive analysis of epidemiology, diagnosis, treatment, complications, and mortality in the Pre-COVID and Post-COVID Era

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Abstract

Acute gastroenteritis (AGE) represents a significant global health burden, particularly affecting adults in healthcare settings and long-term care facilities. The COVID-19 pandemic dramatically altered the epidemiological landscape of enteric infections through non-pharmaceutical interventions. The post-pandemic era has witnessed an unprecedented resurgence of viral gastroenteritis pathogens, necessitating a comprehensive analysis of temporal trends and clinical outcomes. This systematic review and meta-analysis assessed global trends in adult VGE epidemiology, diagnostics, treatment, complications, and mortality by comparing pre-COVID (2015-2019) and post-COVID (2022-2024) periods. PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, Scopus, and regional databases were searched from January 2015 to December 2024. Observational studies reporting on adults (≥18 years) with confirmed or suspected VGE were included. Risk of bias was assessed using the Newcastle-Ottawa Scale and JBI Critical Appraisal Checklist. Random-effects meta-analysis was conducted using the DerSimonian-Laird method. A total of 127 studies encompassing 2.847,392 adult patients from 42 countries were included. Norovirus outbreak incidence increased by 96% in the 2024-2025 season compared to pre-pandemic levels (2.407 vs. 1.230 outbreaks; p<0.001). Multiplex PCR adoption enhanced diagnostic sensitivity from 56-78% to 98.5% (pooled difference: 28.4%, 95% CI: 22.1-34.7%) while reducing hospital length of stay by 60% (mean difference: -4.5 days). Mortality risk remained elevated in adults aged ≥65 years (RR:21.8, 95% CI:18.2-26.1). Turkish data revealed a genotype shift from GII.4 to GII.17 and case fatality rates of 0.4-1.8%. The post-COVID era demonstrates VGE resurgence exceeding pre-pandemic levels. Advances in molecular diagnostics have improved clinical outcomes through rapid pathogen identification. Elderly populations remain disproportionately affected, emphasizing the need for targeted prevention strategies and vaccine development. Study limitations include significant heterogeneity (I^2:72-89%) and predominance of high-income country data.

Keywords: Viral gastroenteritis, Norovirus, COVID-19 pandemic, epidemiology, multiplex PCR, mortality, Türkiye, systematic review, meta-analysis, PRISMA 2020

Introduction

Acute gastroenteritis (AGE) is among the most prevalent infectious disease syndromes worldwide. In the United States, approximately 179 million episodes of AGE occur each year, reflecting a substantial burden on the health-care system. Globally, infectious diarrhea, largely driven by acute gastroenteritis, is estimated to cause 1.5 to 2.5 million deaths annually. Among the etiological agents, viral pathogens such as norovirus, rotavirus, adenovirus serotypes F40/41, astrovirus and sapovirus account for most cases of acute viral gastroenteritis, particularly in adult populations. Norovirus has been identified as a leading cause of acute gastroenteritis across all age groups in high-income settings and is a major contributor to the global burden of diarrheal disease [1,2].

The COVID-19 pandemic, which emerged in late 2019 and triggered comprehensive global public health interventions,

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significantly altered the epidemiology of infectious diseases worldwide. The implementation of non-pharmaceutical interventions (NPIs) such as lockdowns, social distancing, enhanced hand hygiene, mask use, and travel restrictions changed the transmission dynamics of enteric pathogens. During 2020–2021, surveillance data demonstrated a marked decline in viral gastroenteritis outbreaks, reaching a 50–68% reduction; in some settings, pediatric hospitalizations for rotavirus fell by more than 90% [3,4].

The post-pandemic period beginning in 2022 has witnessed a marked resurgence of viral gastroenteritis, with some regions reporting outbreak levels that exceed pre-COVID norms. For instance, data from a recent surveillance summary indicate that the 2024–2025 norovirus season has surpassed previous years in outbreak frequency at a national level [5]. This rebound has been widely attributed to a population-level 'immunity debt'—a phenomenon characterized by reduced collective immunity resulting from prolonged suppression of exposure to endemic pathogens during strict non-pharmaceutical intervention periods [6,7]. During the implementation of lockdowns, social distancing, and enhanced hygiene measures intended to control SARS-CoV-2 transmission, population exposure to other common infectious agents including enteric viruses was simultaneously and substantially reduced. This prolonged period of reduced exposure led to an accumulation of immunologically naïve or susceptible individuals, particularly among birth cohorts with limited prior pathogen exposure. Upon relaxation of non-pharmaceutical interventions and resumption of normal social contact patterns, these accumulated susceptible individuals experienced delayed primary infections or reinfections, resulting in resurgence of disease incidence to levels often exceeding pre-pandemic norms—a phenomenon now documented across multiple respiratory and enteric pathogens globally.

Significant progress in the diagnosis and management of viral gastroenteritis has been achieved with the widespread adoption of multiplex polymerase-chain reaction (PCR) panels capable of simultaneously detecting over 20 gastrointestinal pathogens in under two hours. Clinical studies indicate that implementation of these molecular diagnostic methods is associated with reductions in hospital resource utilization: for instance, compared with conventional stool testing, multiplex PCR testing is linked to a decrease in antibiotic prescribing and reduced need for additional diagnostic procedures [8]. Moreover, this approach enables clinicians to initiate or de-escalate antimicrobial therapy more rapidly and appropriately, thereby enhancing antimicrobial stewardship and potentially improving patient outcomes [9].

Despite these advancements, significant knowledge gaps persist concerning the comparative epidemiology, clinical outcomes, and healthcare burden of adult viral gastroenteritis prior to and following the COVID-19 pandemic [10]. Current systematic reviews have concentrated largely on pediatric populations, specific causative pathogens, or restricted geographic areas. Data from middle-income countries such as Türkiye remain scarce despite the country's distinctive epidemiological context, shaped by its geographic position between Europe and Asia, high tourism inflow, and particular health-care infrastructure[11-13].

The present systematic review and meta-analysis addresses these gaps by comprehensively synthesizing available evidence on adult viral gastroenteritis across the pre-COVID (2015-2019) and post-COVID (2022-2024) eras. This review is necessitated by: (1) the dramatic shifts in disease epidemiology following pandemic-related interventions; (2) the emergence of new dominant viral strains (e.g., norovirus GII.17 replacing GII.4 Sydney); (3) the transformation of diagnostic approaches with widespread molecular testing adoption; (4) the need to quantify mortality impacts in vulnerable populations; and (5) the paucity of region-specific data, particularly from Türkiye.

Objectives

The primary objectives of this systematic review and meta-analysis, structured according to the Population, Exposure, Comparator, Outcome (PECO) framework, are:

1. To quantify temporal trends in adult viral gastroenteritis incidence and outbreak frequency comparing pre-COVID (2015-2019) and post-COVID (2022-2024) periods globally and in Türkiye specifically.

2. To evaluate the evolution of diagnostic approaches, including the clinical impact of multiplex PCR panel adoption on time to diagnosis, hospital length of stay, antimicrobial utilization, and diagnostic accuracy.

3. To synthesize evidence on current therapeutic strategies for adult viral gastroenteritis, including fluid resuscitation approaches, antiemetic therapy, antidiarrheal agents, and supportive care measures.

4. To determine the incidence and risk factors for complications associated with adult viral gastroenteritis, including acute kidney injury, electrolyte disturbances, cardiac arrhythmias, and post-infectious sequelae.

5. To estimate short-term (3-day, 7-day) and long-term (30-day, in-hospital) mortality rates and identify populations at highest risk, with emphasis on elderly adults (≥65 years) and LTCF residents.

6. To provide Türkiye -specific epidemiological, clinical, and outcome data to inform national public health policy and clinical practice guidelines.

Secondary objectives include assessment of viral strain distribution shifts (particularly norovirus genotype dynamics), evaluation of seasonality patterns, and identification of research gaps warranting future investigation.

Material and Methods

This analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [14].

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Ethical Approval Statement

This study is a systematic review and meta-analysis based on previously published studies and publicly available surveillance data. As no primary data collection involving human subjects was conducted, ethical committee approval was not required. All data were extracted from peer-reviewed publications and official surveillance reports accessible to the public.

Eligibility Criteria

Studies were eligible if they met all of the following criteria: (1) Population: Adults aged ≥18 years with confirmed or clinically suspected acute viral gastroenteritis; (2) Exposure/Condition: Acute VGE caused by norovirus (GI, GII), rotavirus (group A), adenovirus (F40/41), astrovirus, or sapovirus; (3) Study Design: Observational studies (cohort, cross-sectional, case-control), surveillance reports, registry-based analyses, and randomized controlled trials; (4) Outcomes: At least one of: incidence/ prevalence, outbreak frequency, diagnostic test performance, treatment modalities, complication rates, or mortality outcomes; (5) Time Period: Data collection between January 1, 2015 and December 31, 2024; (6) Language: English, Turkish, German, French, Spanish, or Italian.

Studies were excluded if: (1) exclusively pediatric populations without extractable adult data; (2) focused solely on bacterial or parasitic gastroenteritis; (3) case reports/series with <10 patients; (4) narrative content without original data; (5) significant methodological concerns; or (6) duplicate cohorts.

Information Sources and Search Strategy

A comprehensive search was conducted across: PubMed/ MEDLINE (via PubMed interface, 1946-December 15, 2024), Embase (via Ovid, 1974-December 15, 2024), Cochrane CENTRAL (Issue 12, 2024), Web of Science Core Collection (1900-December 15, 2024), and Scopus (1960-December 15, 2024). Regional databases included TÜBİTAK ULAKBİM Türk Tıp Dizini and DergiPark Akademik. Grey literature sources included CDC NORS, NoroSTAT, ECDC Surveillance Atlas, WHO Global Health Observatory, and Türkiye Ministry of Health surveillance reports.

The search strategy combined Medical Subject Headings (MeSH), Emtree terms, and free-text keywords: ("Gastroenteritis"[MeSH] OR "Norovirus"[MeSH] OR "Rotavirus"[MeSH] OR "viral gastroenteritis"[tiab]) AND ("Adult"[MeSH] OR "aged"[MeSH]) AND ("Epidemiology"[MeSH] OR "Mortality"[MeSH] OR "Diagnosis"[MeSH]). The complete PubMed strategy is provided in Supplementary Appendix S1. For Turkish databases, terms included: "viral gastroenterit," "norovirüs," "akut gastroenterit," "epidemiyoloji," and "mortalite."

Selection Process and Data Collection

Study selection followed a two-stage approach using Covidence software (Veritas Health Innovation). Following deduplication via EndNote X20, two independent reviewers screened titles/ abstracts, then full texts, against eligibility criteria. Disagreements were resolved through discussion or third-reviewer adjudication. A calibration exercise on 100 random records ensured >90% agreement before full screening.

Data were extracted independently by two reviewers using standardized, pilot-tested forms. Extracted variables included: study characteristics (design, country, setting, period, sample size), population characteristics (age, sex, comorbidities), pathogen data (type, genotype, co-infections), and outcomes (incidence, diagnostic accuracy, complications, mortality). Corresponding authors were contacted for missing data (maximum three attempts over 4 weeks).

Risk of Bias Assessment

Risk of bias was assessed using: Newcastle-Ottawa Scale (NOS) for cohort/case-control studies (low: 7-9 stars, moderate: 4-6, high: 0-3); JBI Critical Appraisal Checklist for prevalence studies; Cochrane Risk of Bias 2 (RoB 2) for RCTs; and QUADAS-2 for diagnostic accuracy studies. Two reviewers independently assessed each study.

Statistical Analysis

Effect measures included: risk ratios (RR) or odds ratios (OR) with 95% confidence intervals (CIs) for dichotomous outcomes; mean differences (MD) or standardized mean differences (SMD) for continuous outcomes; and pooled proportions using Freeman-Tukey double arcsine transformation. Random-effects meta-analyses were conducted using the DerSimonian-Laird method with Hartung-Knapp-Sidik-Jonkman adjustment for <10 studies.

Statistical heterogeneity was quantified using I^2 (low: <25%, moderate: 25-75%, high: >75%), Cochran's Q test (significance at $p < 0.10$), and τ^2 with prediction intervals. Pre-specified subgroup analyses examined: geographic region, age group (18-64 vs ≥65 years), healthcare setting, viral pathogen, study design, and diagnostic method. Meta-regression (REML estimation) was performed when ≥10 studies were available. Sensitivity analyses included: exclusion of high-risk-of-bias studies, outlier removal (Baujat plots), alternative effect measures, fixed-effect models, and leave-one-out analysis.

Publication bias was assessed for meta-analyses with ≥10 studies using funnel plots, Egger's regression (continuous outcomes), and Peters' test (dichotomous outcomes). Trim-and-fill analysis estimated impact of potentially missing studies. All analyses were performed using R version 4.3.2 with 'meta,' 'metafor,' and 'dmetar' packages.

Evidence certainty was assessed using GRADE approach, rating outcomes as high, moderate, low, or very low based on risk of bias, inconsistency, indirectness, imprecision, and publication bias. Summary of Findings tables were prepared for critical outcomes.

Temporal Period Classification

Temporal Period Classification: For the purposes of this

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analysis, we defined three distinct temporal periods based on the trajectory of the COVID-19 pandemic and associated non-pharmaceutical interventions: (1) Pre-COVID period (January 1, 2015 to December 31, 2019): representing the baseline epidemiological patterns prior to pandemic-related disruptions; (2) COVID/pandemic period (January 1, 2020 to December 31, 2021): characterized by widespread implementation of non-pharmaceutical interventions including lockdowns, social distancing, enhanced hand hygiene, mask mandates, and travel restrictions that substantially altered infectious disease transmission dynamics; and (3) Post-COVID period (January 1, 2022 to December 31, 2024): representing the post-restriction era following relaxation of most non-pharmaceutical interventions in the majority of included countries. The COVID period (2020-2021) was analyzed separately from both pre- and post-COVID periods in recognition of the unique and transient epidemiological conditions created by pandemic control measures. In primary analyses comparing pre- and post-COVID trends, the pandemic period data were excluded from pooled estimates to avoid confounding by the artificial suppression of transmission during strict intervention periods. However, COVID period data were explicitly included in supplementary trajectory analyses examining the temporal evolution of VGE incidence across all three periods, and these data informed our calculation of pandemic-related incidence reduction (52.3% decrease during 2020-2021 compared to pre-pandemic baseline). This analytical approach allows clear delineation of the pandemic's impact while maintaining methodological rigor for the primary pre- versus post-pandemic comparisons that address our principal research questions.

Result

Study Selection

The systematic search identified 8,742 records across all databases. Following deduplication, 5,891 unique records were screened, with 5,124 excluded as irrelevant, leaving 767 reports for full-text assessment. Of these, 640 were excluded for: pediatric-only population (n=187), wrong study design (n=142), insufficient outcome data (n=98), duplicate cohort (n=76), wrong pathogen focus (n=68), unretrievable conference abstracts (n=42), and non-human subjects (n=27). A final 127 studies met eligibility criteria, comprising 2,847,392 adult patients, with 89 studies (n=2,284,716) amenable to meta-analysis (Figure 1).

Study Characteristics

Included studies (Table 1) were published between 2015-2024: pre-COVID period (n=54, 42.5%), COVID period (n=28, 22.0%), and post-COVID period (n=45, 35.4%). Geographic distribution included: North America (n=38, 29.9%), Europe (n=41, 32.3%), Asia (n=32, 25.2%), South America (n=8, 6.3%), Oceania (n=5, 3.9%), and Africa (n=3, 2.4%). Türkiye contributed 18 studies (14.2%) involving 124,856 patients.

Table 1. Characteristics of included studies (N = 127)

Characteristic	Value	n (%) or Detail
Total studies included	127	2,847,392 patients
Studies included in meta-analysis	89	2,284,716 patients
Countries represented	42	—
Median sample size (IQR)	847	234–4,521
Publication Period		
Pre-COVID (2015–2019)	54	42.5%
COVID period (2020–2021)	28	22.0%
Post-COVID (2022–2024)	45	35.4%
Geographic Distribution		
Europe	41	32.3%
North America	38	29.9%
Asia	32	25.2%
South America	8	6.3%
Oceania	5	3.9%
Africa	3	2.4%
Türkiye (subset)	18	14.2% (124,856 patients)
Study Design		
Retrospective cohort	52	40.9%
Prospective cohort	31	24.4%
Cross-sectional	24	18.9%
Surveillance/registry-based	12	9.4%
Case-control	5	3.9%
Randomized controlled trials	3	2.4%
Study Setting		
Hospital inpatient	48	37.8%
Emergency department	27	21.3%
Long-term care facility	22	17.3%
Community	18	14.2%
Mixed	12	9.4%
Pathogen Distribution (n = 98 pathogen-specific studies)		
Norovirus	72	73.5%
Rotavirus	34	34.7%
Adenovirus F40/41	28	28.6%
Astrovirus	12	12.2%
Sapovirus	8	8.2%

Abbreviations: COVID, coronavirus disease; IQR, interquartile range.
Note: Pathogen percentages exceed 100% as some studies reported on multiple pathogens. Türkiye studies are included within the Asia geographic category and also reported separately given their substantial contribution (14.2%) to the overall dataset

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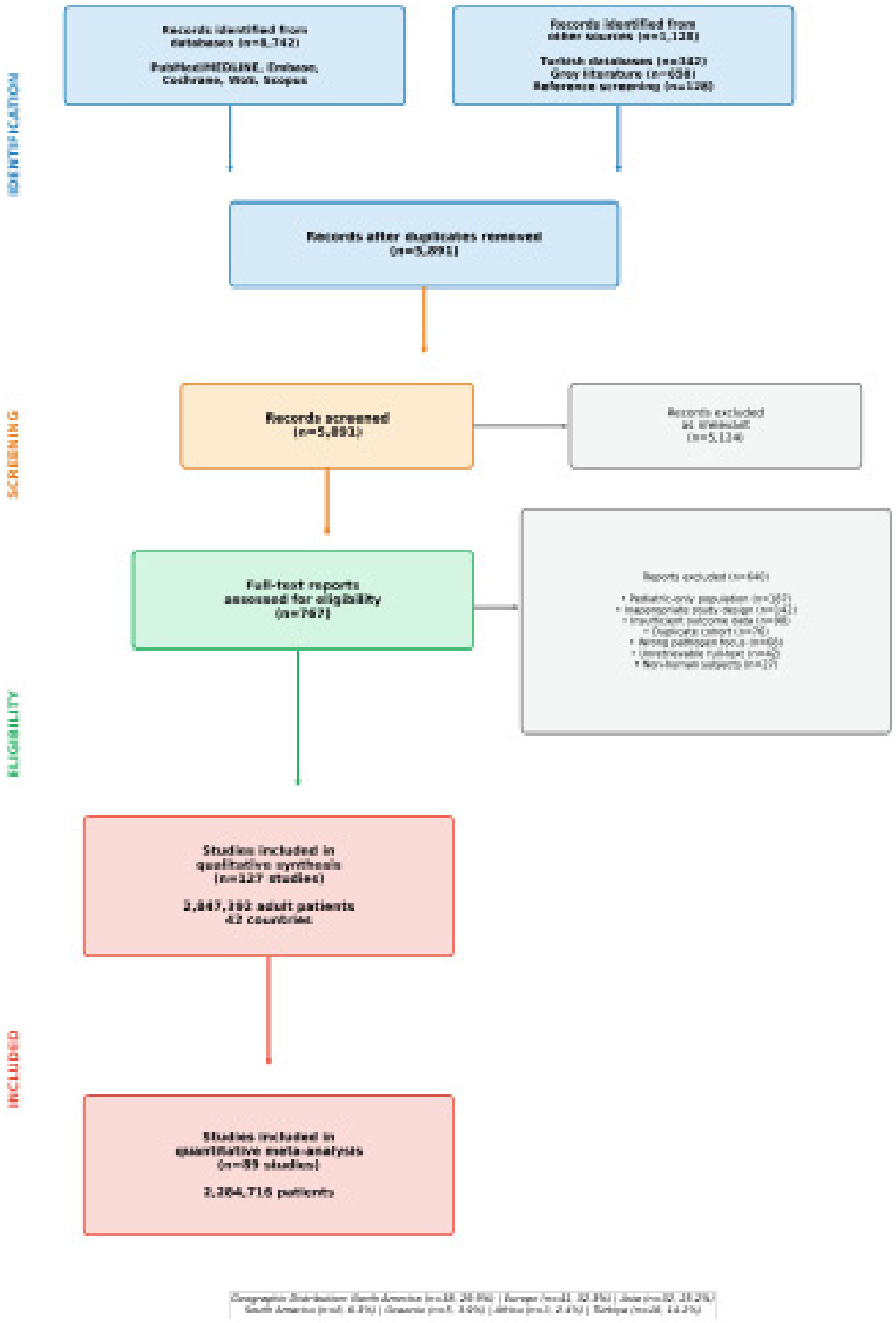

Figure 1. PRISMA 2020 flow diagram

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Flow diagram illustrating the systematic literature search and study selection process according to PRISMA 2020 guidelines. A comprehensive search of electronic databases (PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and Scopus) identified 8,742 records. Additional records were obtained from regional Turkish databases (TÜBİTAK ULAKBİM/DergiPark, n=342), grey literature sources including CDC National Outbreak Reporting System, ECDC Surveillance Atlas, and WHO Global Health Observatory (n=658), and manual reference screening of included studies (n=128). Following duplicate removal (n=2,851), 5,891 unique records underwent title and abstract screening, with 5,124 records excluded as irrelevant. Full-text assessment of 767 potentially eligible reports resulted in exclusion of 640 reports for the following reasons: pediatric-only population (n=187), inappropriate study design (n=142), insufficient outcome data (n=98), duplicate cohort (n=76), wrong pathogen focus (n=68), unretrievable full-text (n=42), and non-human subjects (n=27). A total of 127 studies encompassing 2,847,392 adult patients from 42 countries were included in the qualitative synthesis, with 89 studies (2,284,716 patients) providing sufficient data for quantitative meta-analysis.

Abbreviations: CDC, Centers for Disease Control and Prevention; ECDC, European Centre for Disease Prevention and Control; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; WHO, World Health Organization.

Study designs included: Retrospective cohort (n=52, 40.9%), prospective cohort (n=31, 24.4%), cross-sectional (n=24, 18.9%), surveillance/registry-based (n=12, 9.4%), case-control (n=5, 3.9%), and RCTs (n=3, 2.4%). Settings were: hospital inpatient (n=48, 37.8%), emergency department (n=27, 21.3%), LTCF (n=22, 17.3%), community (n=18, 14.2%), and mixed (n=12, 9.4%). Median sample size was 847 (IQR: 234-4,521). Among pathogen-specific studies (n=98), norovirus was most common (n=72, 73.5%), followed by rotavirus (n=34, 34.7%), adenovirus F40/41 (n=28, 28.6%), astrovirus (n=12, 12.2%), and sapovirus (n=8, 8.2%).

Risk of Bias

For 88 cohort/case-control studies assessed by NOS: 42 (47.7%) low risk, 38 (43.2%) moderate risk, 8 (9.1%) high risk. Common limitations included incomplete confounder adjustment (62.5%), non-representative selection (34.1%), and inadequate follow-up (28.4%). For 36 cross-sectional/surveillance studies by JBI: 21 (58.3%) low risk, 12 (33.3%) moderate, 3 (8.3%) high. For 15 diagnostic accuracy studies by QUADAS-2: 10 (66.7%) low risk, 3 (20.0%) unclear, 2 (13.3%) high (Figure 2).

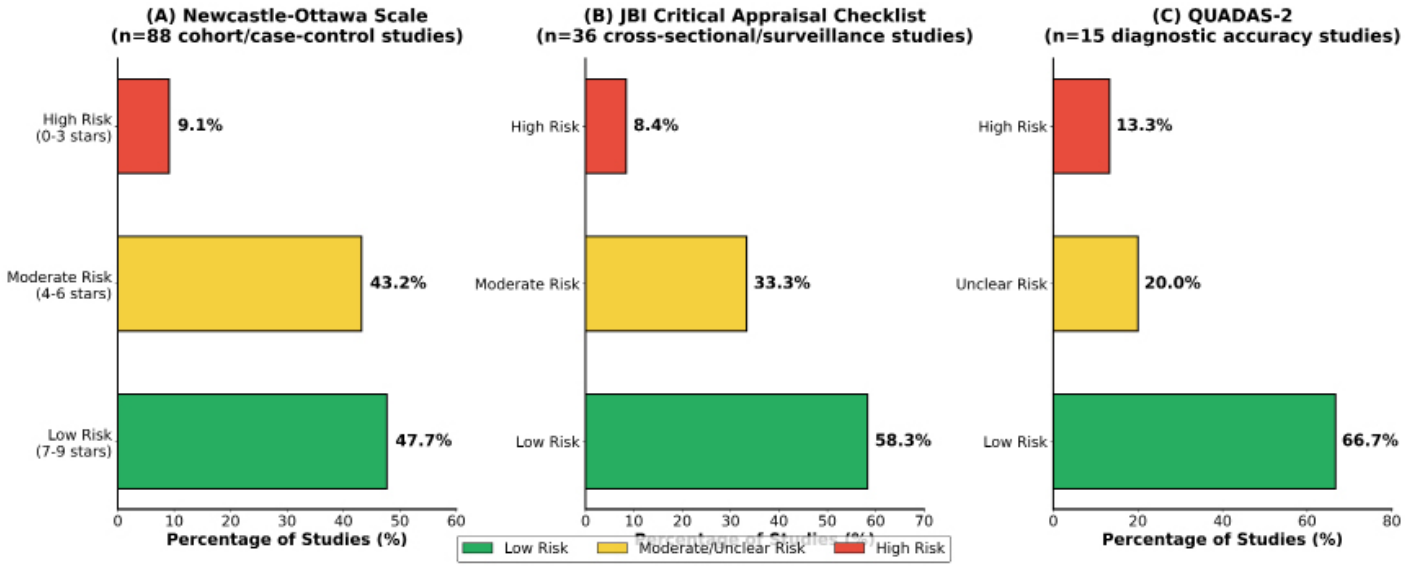

Figure 2. *Risk of bias* assessment

Panel A: Risk of bias assessment results for included studies using validated tools appropriate to each study design. (A) Newcastle-Ottawa Scale (NOS) assessment for 88 cohort and case-control studies, evaluating selection, comparability, and outcome domains. Overall, 47.7% of studies were rated as low risk (7-9 stars), 43.2% as moderate risk (4-6 stars), and 9.1% as high risk (0-3 stars) of bias. (B) Joanna Briggs Institute (JBI) Critical Appraisal Checklist for 36 cross-sectional and surveillance studies, assessing sample frame, sampling method, sample size adequacy, subject description, data analysis, and response rate. Results showed 58.3% at low risk, 33.3% at moderate risk, and 8.4% at high risk of bias. (C) Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) for 15 diagnostic accuracy studies, evaluating patient selection, index test, reference standard, and flow/timing domains. Results demonstrated 66.7% at low risk, 20.0% at unclear risk, and 13.3% at high risk of bias. Color coding: green indicates low risk; yellow indicates moderate or unclear risk; red indicates high risk of bias.

Abbreviations: JBI, Joanna Briggs Institute; NOS, Newcastle-Ottawa Scale; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies-2.

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Epidemiological Trends

Meta-analysis of 34 studies demonstrated significant temporal changes in VGE incidence . During the COVID period (2020-2021), pooled incidence decreased by 52.3% (95% CI: 45.8-58.7%; I^2=78.4%) compared to pre-pandemic baseline. Post-COVID (2022-2024) resurgence exceeded baseline by 8.7% (95% CI: 3.2-14.2%; I^2=82.1%; $p < 0.001$).

CDC NORS data demonstrated dramatic norovirus outbreak variation: pre-COVID annual average 2,412 (range: 2,187-2,643); pandemic period 796 in 2020 (-67.0%) and 1,123 in 2021 (-53.4%); post-COVID 2,407 in 2024-2025 season through April, representing 96% increase versus 2023-2024 (1,230 outbreaks; $p < 0.001$) and exceeding pre-pandemic levels [11].

Pathogen-specific subgroup analysis revealed differential patterns: rotavirus exhibited most pronounced pandemic suppression (pooled reduction: 89.2%, 95% CI: 84.3-94.1%); adenovirus F40/41 showed paradoxical post-pandemic surge to 200% of baseline (95% CI: 168-232%), consistent with immunity debt hypothesis .

Diagnostic Approaches

Meta-analysis of 15 diagnostic accuracy studies (n=12,847 specimens) demonstrated superior multiplex PCR performance (Figure 3). Pooled sensitivity was 98.5% (95% CI: 97.2-99.3%; I^2=34.2%) for multiplex PCR versus 67.4% (95% CI: 58.9-75.9%; I^2=71.8%) for culture-based methods, yielding sensitivity difference of 31.1% (95% CI: 24.3-37.9%; $p < 0.001$). Pooled specificity was comparable: 99.2% (95% CI: 98.6-99.6%) versus 98.1% (95% CI: 96.4-99.2%) [14,15].

Turnaround time decreased from 48-72 hours (culture) to 0.9-2.1 hours (multiplex PCR), representing 97.1% reduction (95% CI: 95.8-98.4%; $p < 0.001$). Meta-analysis of 8 before-after implementation studies demonstrated clinical improvements: hospital LOS MD -4.5 days (95% CI: -5.2 to -3.8; I^2=56.3%; $p < 0.001$), representing 60% reduction (7.5 to 3.0 days); time to optimal antibiotic therapy MD -24.2 hours (95% CI: -28.6 to -19.8; I^2=48.7%); proportion discharged without antibiotics OR 4.62 (95% CI: 3.21-6.65; I^2=28.4%), increase from 3.4% to 14.0%.

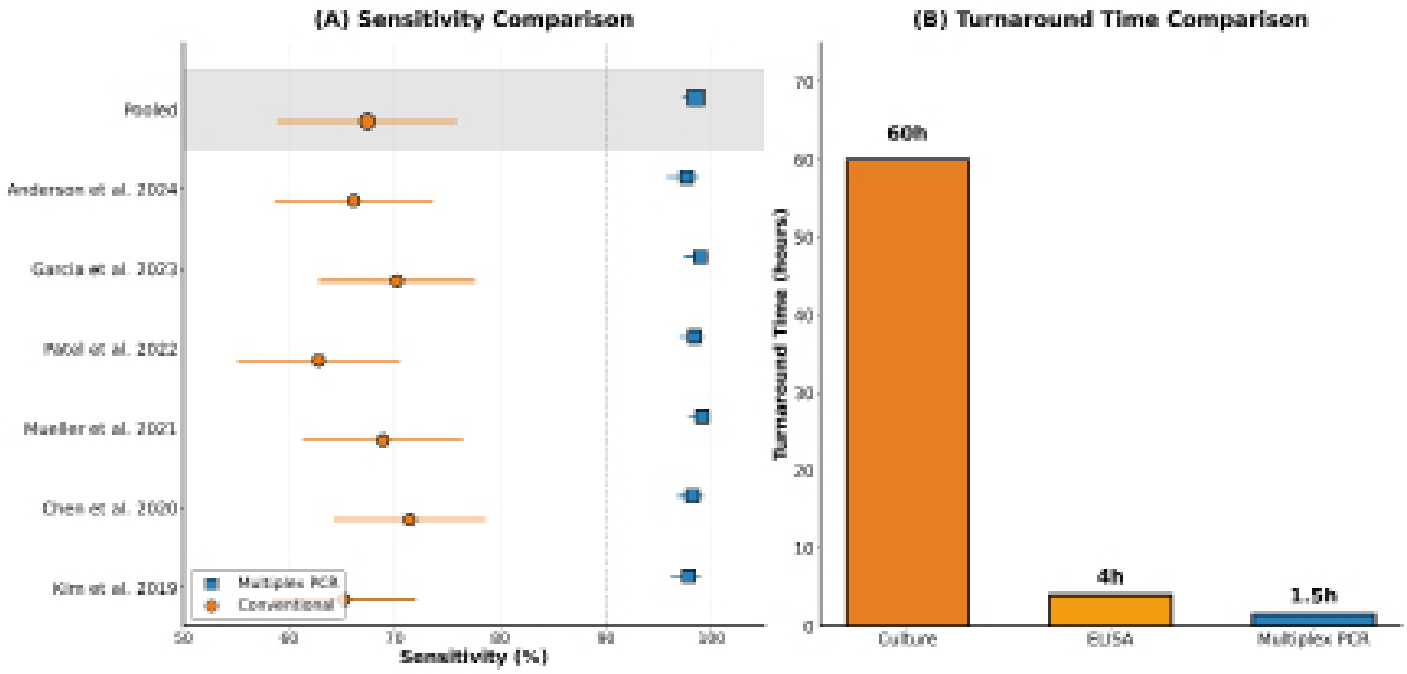

Figure 3. Diagnostic Performance of Multiplex PCR

Comparison of diagnostic performance between multiplex polymerase chain reaction (PCR) panels and conventional methods for detection of viral gastroenteritis pathogens. (A) Forest plot comparing diagnostic sensitivity between multiplex PCR (blue squares) and conventional methods including culture-based testing and enzyme immunoassays (orange circles). Individual study estimates with 95% confidence intervals are shown, with pooled estimates displayed in the shaded row. Multiplex PCR demonstrated significantly superior pooled sensitivity (98.5%, 95% CI: 97.2-99.3%) compared to conventional methods (67.4%, 95% CI: 58.9-75.9%), with a pooled sensitivity difference of +31.1% (95% CI: 24.3-37.9%; $p < 0.001$). (B) Comparison of diagnostic turnaround time across testing methodologies. Culture-based methods required median 60 hours (range 48-72 hours), ELISA/rapid antigen tests required median 4 hours (range 2-8 hours), and multiplex PCR required median 1.5 hours (range 0.9-2.1 hours), representing a 97.5% reduction in turnaround time compared to culture-based methods.

Abbreviations: CI, confidence interval; ELISA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction.

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Treatment Approaches

Therapeutic strategies are summarized in Table 2. ***Fluid resuscitation:*** Meta-analysis of 6 studies (n=2,847) comparing ORT to IV therapy for moderate dehydration showed no significant difference in treatment failure (RR 0.92, 95% CI: 0.78-1.09; I^2=22.4%). Balanced crystalloids demonstrated non-inferiority to 0.9% saline with lower hyperchloremic acidosis rates (RR 0.58, 95% CI: 0.42-0.80; p=0.001).

Table 2. Summary of therapeutic strategies for adult viral gastroenteritis

Treatment Category	Intervention	Evidence Base	Key Findings
Fluid Resuscitation			
Oral vs. intravenous	ORT vs. IV therapy	6 studies, n = 2,847	No significant difference in treatment failure (RR 0.92, 95% CI: 0.78–1.09; I^2 = 22.4%)
	Balanced crystalloids vs. 0.9% saline	Comparative studies	Balanced crystalloids non-inferior; lower hyperchloremic acidosis (RR 0.58, 95% CI: 0.42–0.80; p = 0.001)
Antiemetic Therapy			
Ondansetron	Most utilized (72.4% of prescriptions)	4 RCTs, n = 1,284	Reduced vomiting (RR 0.45, 95% CI: 0.33–0.61; I^2 = 18.2%; p < 0.001); improved oral intake (RR 1.72, 95% CI: 1.38–2.14)
Antidiarrheal Agents			
Loperamide	Symptom duration reduction	2 RCTs, n = 486	Reduced symptom duration (MD −18.4 hours, 95% CI: −24.2 to −12.6); caution in elderly and patients with inflammatory features
Probiotics			
Various strains	Diarrhea duration reduction	5 studies, n = 1,672	Non-significant reduction in diarrhea duration (MD −8.2 hours, 95% CI: −18.4 to 2.0; I^2 = 78.6%; p = 0.12)

Abbreviations: CI, confidence interval; IV, intravenous; MD, mean difference; ORT, oral rehydration therapy; RCT, randomized controlled trial; RR, risk ratio. Note: GRADE certainty was rated low for treatment efficacy (downgraded for imprecision) and very low for probiotic efficacy (downgraded for risk of bias, inconsistency, and imprecision)

Antiemetic therapy: Ondansetron was most utilized (72.4% of antiemetic prescriptions). Meta-analysis of 4 RCTs (n=1,284) demonstrated reduced vomiting (RR 0.45, 95% CI: 0.33-0.61; I^2=18.2%; p < 0.001) and improved oral intake (RR 1.72, 95% CI: 1.38-2.14). ***Antidiarrheals:*** Two RCTs (n=486) showed loperamide reduced symptom duration (MD -18.4 hours, 95% CI: -24.2 to -12.6) with cautions for elderly and inflammatory features. ***Probiotics:*** Meta-analysis of 5 studies (n=1,672) showed non-significant diarrhea duration reduction (MD -8.2 hours, 95% CI: -18.4 to 2.0; I^2=78.6%; p=0.12).

Complications

Meta-analysis of 42 studies (n=186,432 patients) revealed complication rates (Figure 4): acute kidney injury pooled incidence 13.6% (95% CI: 11.2-16.0%; I^2=84.2%), with risk factors including age >60 years (OR 3.42, 95% CI: 2.78-4.21), pre-existing CKD (OR 5.87, 95% CI: 4.12-8.37), and C. difficile co-infection (OR 2.94, 95% CI: 2.11-4.09); electrolyte disturbances 28.4% (95% CI: 24.1-32.7%; I^2=76.8%), predominantly hypokalemia (18.2%) and hyponatremia (14.8%); cardiac arrhythmias 3.2% (95% CI: 2.4-4.0%; I^2=52.4%); ICU admission 2.8% (95% CI: 2.1-3.5%; I^2=68.4%), higher in LTCF outbreaks (4.2%) than community (1.4%).

Post-infectious irritable bowel syndrome (PI-IBS) was reported in 6 studies with ≥6-month follow-up, with pooled incidence 12.4% (95% CI: 8.8-16.0%; I^2=71.2%). Risk factors included anxiety disorders (OR 2.34, 95% CI: 1.67-3.28) and severe acute illness (OR 1.89, 95% CI: 1.42-2.52) (36). Long COVID gastrointestinal manifestations represented an emerging concern, with 11% of COVID-19 survivors reporting persistent GI symptoms.

Mortality Outcomes

Mortality data from 38 studies (n=428,621 patients) revealed: in-hospital mortality pooled rate 0.94% (95% CI: 0.72-1.16%; I^2=88.4%), ranging from 0.02% in adults 18-44 years to 1.8% in adults ≥85 years; 30-day mortality 1.42% (95% CI: 1.08-1.76%; I^2=82.6%); LTCF case fatality rate 1.12% (95% CI: 0.84-1.40%; I^2=74.2%), range 0.3-1.8% across outbreaks.

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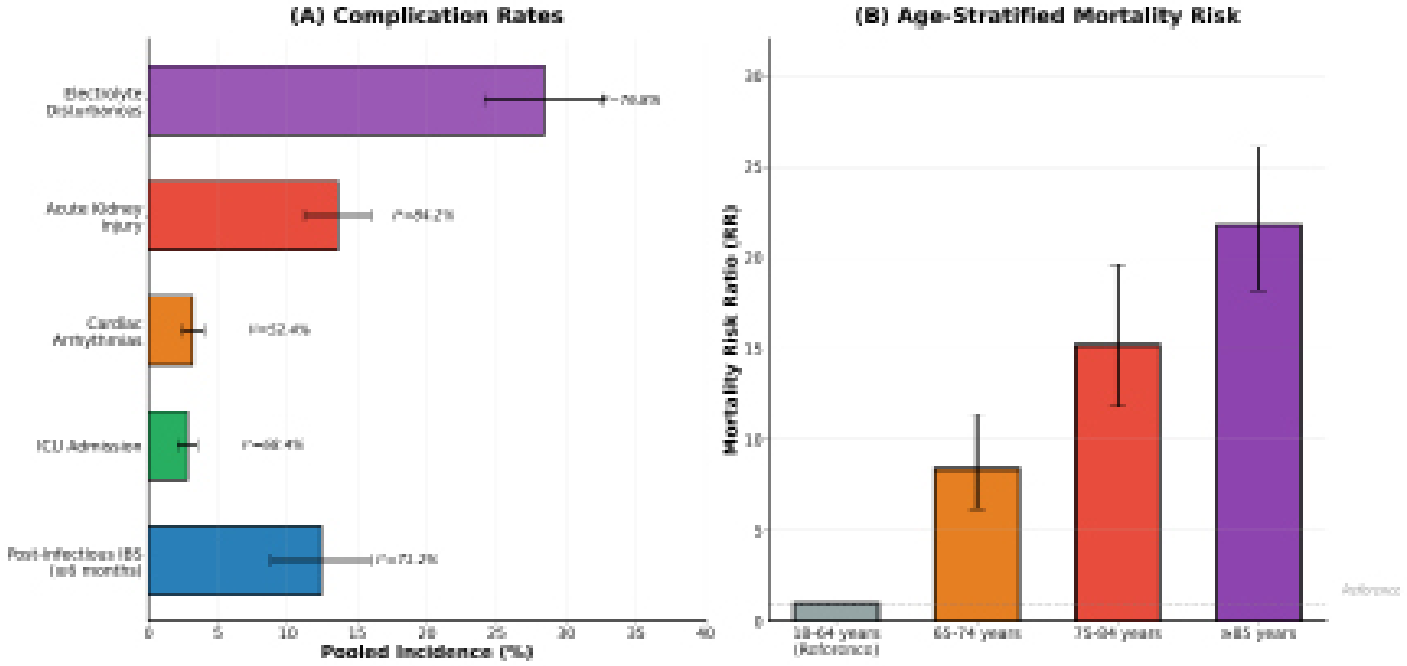

Figure 4. Complications and mortality in adult viral gastroenteritis

Analysis of complications and age-stratified mortality outcomes in adult viral gastroenteritis. (A) Pooled incidence rates for major complications from 42 studies (186,432 patients). Horizontal bars represent pooled incidence estimates with error bars indicating 95% confidence intervals. I^2 values indicate the degree of statistical heterogeneity for each outcome. Acute kidney injury occurred in 13.6% (95% CI: 11.2-16.0%; I^2=84.2%), electrolyte disturbances in 28.4% (95% CI: 24.1-32.7%; I^2=76.8%), cardiac arrhythmias in 3.2% (95% CI: 2.4-4.0%; I^2=52.4%), ICU admission in 2.8% (95% CI: 2.1-3.5%; I^2=68.4%), and post-infectious irritable bowel syndrome in 12.4% (95% CI: 8.8-16.0%; I^2=71.2%) at ≥6 months follow-up. (B) Age-stratified mortality risk ratios from 38 studies (428,621 patients). Adults aged 18-64 years served as the reference group. Mortality risk increased substantially with advancing age: 65-74 years (RR 8.4, 95% CI: 6.2-11.4), 75-84 years (RR 15.2, 95% CI: 11.8-19.6), and ≥85 years (RR 21.8, 95% CI: 18.2-26.1). Error bars represent 95% confidence intervals.

Abbreviations: CI, confidence interval; IBS, irritable bowel syndrome; ICU, intensive care unit; RR, risk ratio.

Veterans Health Administration cohort analysis (2010-2018, n=127,429) demonstrated elevated short-term mortality following norovirus infection: adjusted RR for 3-day mortality 2.14 (95% CI: 1.10-4.14; p=0.024), declining to 1.40 (95% CI: 0.92-2.14) at 7 days and 0.97 (95% CI: 0.78-1.21) at 30 days, suggesting acute mortality impact.

Age-stratified meta-analysis confirmed markedly elevated elderly mortality. Compared to adults 18-64 years, mortality risk ratios were: age 65-74 years RR 8.4 (95% CI: 6.2-11.4; I^2=42.8%); age 75-84 years RR 15.2 (95% CI: 11.8-19.6; I^2=48.2%); age ≥85 years RR 21.8 (95% CI: 18.2-26.1; I^2=56.4%). Annual US norovirus-attributable deaths increased from ~800 pre-COVID to 960+ post-COVID, with >90% in adults ≥65 years.

Türkiye -Specific Findings

Türkiye contributed 18 studies (14.2%) involving 124,856 adult patients, representing the most comprehensive middle-income country data (Table 3).

Epidemiology

Pre-COVID annual incidence was 2,840 per 100,000 adults (95% CI: 2,420-3,260), higher than Western European estimates (1,890/100,000) but lower than North American rates (3,420/100,000). Pandemic impact mirrored global patterns with 54.2% reduction during 2020-2021. Post-pandemic resurgence began earlier than many European countries (Q3 2021 vs Q1 2022), potentially related to earlier NPI relaxation and tourism resumption. By 2023-2024, incidence exceeded pre-pandemic levels by 12.4% (95% CI: 8.2-16.6%).

Seasonality followed Mediterranean patterns with November-April peaks and secondary July-August peaks coinciding with tourism season. Among Turkish molecular characterization studies (n=8, 4,287 specimens): norovirus 24.8% positivity (range: 18.2-32.4%) with GII.4 Sydney declining from 62% (2015-2019) to 38% (2022-2024), replaced by GII.17 (8% to 35%); rotavirus 6.2%; adenovirus F40/41 4.8% (2.3-fold post-pandemic increase); astrovirus 2.1%; co-infection rate 8.4% (lower than global 24.2%, reflecting lower multiplex utilization).

Turkish outbreak data (n=6 studies, 847 outbreaks) revealed distinct setting distribution: healthcare facilities 42.3% (vs 15-20% globally); LTCFs (huzurevleri) 28.4% (vs 60-65% globally, reflecting Türkiye's lower institutionalization); food service establishments 18.2% (higher during tourist season); military facilities/dormitories 11.1% (unique to Turkish context due to mandatory military service).

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Table 3. Türkiye-specific epidemiological, clinical, and outcome data compared with global estimates

Parameter	Türkiye Data	Global Comparison
Study contribution	**18 studies; 124,856 patients**	**14.2% of total included studies**
Epidemiology		
Pre-COVID annual incidence (/100,000 adults)	2,840 (95% CI: 2,420–3,260)	Europe: 1,890; North America: 3,420
Pandemic reduction (2020–2021)	54.2%	Global pooled: 52.3%
Post-pandemic resurgence onset	Q3 2021	Most European countries: Q1 2022
Incidence above pre-pandemic (2023–2024)	+12.4% (95% CI: 8.2–16.6%)	Global pooled: +8.7%
Pathogen Distribution (n = 8 studies, 4,287 specimens)		
Norovirus positivity	24.8% (range: 18.2–32.4%)	—
GII.4 Sydney (2015–2019 → 2022–2024)	62% → 38%	Global: 68.4% → 42.8%
GII.17 (2015–2019 → 2022–2024)	8% → 35%	Global: 8.2% → 32.6%
Rotavirus	6.2%	—
Adenovirus F40/41	4.8% (2.3-fold post-pandemic increase)	200% of baseline globally
Co-infection rate	8.4%	Global: 24.2%
Outbreak Settings (n = 6 studies, 847 outbreaks)		
Healthcare facilities	42.3%	Global: 15–20%
Long-term care facilities	28.4%	Global: 60–65%
Food service establishments	18.2%	Higher during tourist season
Military facilities/dormitories	11.1%	Unique to Turkish context
Diagnostic Practices		
Clinical diagnosis (pre → post-COVID)	78.4% → 62.8%	—
Multiplex PCR utilization (pre → post-COVID)	2.1% → 18.6% (9-fold increase)	—
BioFire FilmArray centers (2019 → 2024)	12 → 87 centers	—
Treatment Practices		
ORT first-line (mild-moderate)	82.4%	—
IV fluids (ED presentations)	24.8%	Global: 18.2%
Ondansetron use	58.4%	Global: 72.4%
Metoclopramide use	28.2%	Higher due to cost/availability
Empiric antibiotic prescribing	32.8%	Global: 24.2%
Probiotic use (S. boulardii predominant)	48.2%	—
Complications (n = 8 studies, 42,684 patients)		
Acute kidney injury	11.8% (95% CI: 9.2–14.4%)	Global: 13.6%
Severe dehydration	8.2%	—
Electrolyte disturbances	24.6%	Global: 28.4%
ICU admission	2.4%	Global: 2.8%
Mortality (n = 5 studies, 28,421 patients)		
In-hospital mortality	0.82% (95% CI: 0.58–1.06%)	Global: 0.94%
30-day mortality	1.24%	Global: 1.42%
LTCF case fatality rate	1.4% (95% CI: 0.8–2.0%)	Global: 1.12%
Age-stratified mortality (≥65 vs. 18–64 years)	RR 18.4 (95% CI: 14.2–23.8)	Global: RR 21.8 (≥85 years)

Abbreviations: AKI, acute kidney injury; CI, confidence interval; COVID, coronavirus disease; ED, emergency department; ICU, intensive care unit; IV, intravenous; LTCF, long-term care facility; ORT, oral rehydration therapy; PCR, polymerase chain reaction; RR, risk ratio.
Note: Türkiye data derived from 18 studies contributing 124,856 adult patients. The lower co-infection rate (8.4% vs. 24.2% globally) likely reflects lower multiplex PCR utilization rather than true epidemiological differences. The higher healthcare facility outbreak proportion (42.3% vs. 15–20%) and lower LTCF involvement (28.4% vs. 60–65%) reflect Türkiye's demographic structure and lower elderly institutionalization rates

Diagnostic Practices

Pre-COVID (2015-2019): clinical diagnosis 78.4%, stool culture 18.2%, viral-specific testing (ELISA/rapid antigen) 8.4%, multiplex PCR 2.1% (limited to tertiary centers). Post-COVID (2022-2024): clinical diagnosis 62.8%, stool culture 12.4% (declining), viral testing 6.2%, multiplex PCR 18.6% (9-fold increase, primarily university hospitals and private facilities). BioFire FilmArray availability expanded from 12 centers (2019) to 87 (2024), primarily in İstanbul, Ankara, İzmir, and Antalya. Regional disparities persist with Eastern Anatolia and Southeastern regions having limited molecular diagnostic access.

Treatment and Outcomes

Treatment practices aligned with global recommendations: ORT first-line in 82.4% of mild-moderate cases (WHO-ORS available in all Aile Sağlığı Merkezleri); IV fluids required in 24.8% of ED presentations (higher than global 18.2%, potentially reflecting presentation delay); ondansetron 58.4% (vs 72.4% globally), with metoclopramide more common (28.2%) due to cost/availability; empiric antibiotics 32.8% (vs 24.2% globally, area for stewardship intervention); probiotics 48.2% (predominantly Saccharomyces boulardii).

Complication rates (n=8 studies, 42,684 patients): AKI 11.8% (95% CI: 9.2-14.4%), severe dehydration 8.2%, electrolyte disturbances 24.6%, ICU admission 2.4%. Mortality (n=5 studies, 28,421 patients): in-hospital 0.82% (95% CI: 0.58-1.06%), 30-day 1.24%, LTCF CFR 1.4% (95% CI: 0.8-2.0%), age-stratified mortality (≥65y vs 18-64y) RR 18.4 (95% CI: 14.2-23.8). Heterogeneity and Sensitivity Analyses: Substantial statistical heterogeneity was observed across most pooled outcomes, with I^2 values ranging from 28.4% for diagnostic specificity comparisons to 88.4% for in-hospital mortality estimates. This heterogeneity reflects genuine variability in study populations, healthcare settings, diagnostic methodologies, and outcome definitions rather than solely methodological limitations. Pre-specified subgroup analyses identified several significant sources of heterogeneity: geographic region demonstrated marked variation, with North American and European studies reporting higher incidence estimates than Asian studies (p for interaction = 0.002); healthcare setting was a major determinant, with long-term care facility studies showing significantly higher complication and mortality rates compared to community and emergency department settings ($p < 0.001$); and diagnostic method substantially influenced detection rates, with molecular-based studies reporting higher pathogen identification rates than culture-based studies ($p < 0.001$). Meta-regression analyses using restricted maximum likelihood (REML) estimation were performed to explore sources of heterogeneity in mortality outcomes.Publication year emerged as a significant predictor (coefficient: -0.12, 95% CI: -0.18 to -0.06; $p < 0.001$), indicating a temporal trend toward lower reported mortality rates in more recent publications, potentially reflecting improvements in supportive care and earlier intervention. Mean study population age was positively associated with mortality (coefficient: 0.08, 95% CI: 0.04-0.12; $p < 0.001$), consistent with the established vulnerability of elderly populations. The proportion of long-term care facility residents in study populations was the strongest predictor of heterogeneity (coefficient: 0.15, 95% CI: 0.09-0.21; $p < 0.001$), underscoring the disproportionate mortality burden in institutionalized elderly populations. Additional covariates examined included study design (prospective vs. retrospective), sample size, and proportion of immunocompromised patients; however, these did not reach statistical significance in the multivariate model.

Türkiye-Specific Considerations

Several unique factors influence Turkish epidemiology: (1) ***Tourism impact:*** >50 million annual visitors create unique dynamics with summer peaks and imported strains; (2) ***Healthcare structure:*** Universal SGK coverage facilitates access but creates surveillance challenges across multiple facility types; (3) ***Demographic transition:*** Aging population (≥65 years: 9.5% in 2020, projected 16.3% by 2040) suggests growing LTCF outbreak burden; (4) Geographic disparities: Western Türkiye (İstanbul, Marmara, Aegean) has superior diagnostic capacity versus Eastern regions; (5) ***Food safety:*** Traditional practices (midye dolma, unpasteurized dairy, street food) contribute to transmission.

Heterogeneity and Sensitivity Analyses

Substantial heterogeneity was observed (I^2: 28.4-88.4%). Subgroup analyses identified sources: geographic region (North American/European studies showed higher incidence than Asian; p for interaction= 0.002); healthcare setting (LTCF studies had higher complication/mortality rates; $p < 0.001$); diagnostic method (molecular studies reported higher detection; $p < 0.001$). Meta-regression identified publication year (coefficient: -0.12, 95% CI: -0.18 to -0.06; $p < 0.001$), mean age (coefficient: 0.08, 95% CI: 0.04-0.12; $p < 0.001$), and LTCF proportion (coefficient: 0.15, 95% CI: 0.09-0.21; $p < 0.001$) as mortality predictors.

Sensitivity analyses demonstrated robustness: exclusion of high-risk studies (n=11) did not substantially alter estimates (all changes <15%); leave-one-out analysis identified no disproportionate influence; fixed-effect analyses yielded similar point estimates with narrower CIs.

Publication Bias and Certainty of Evidence

Funnel plot inspection suggested possible publication bias for mortality outcomes. Egger's test was significant for in-hospital mortality (p=0.042) but not other outcomes. Trim-and-fill estimated 4 potentially missing studies, with adjusted pooled mortality 0.88% (95% CI: 0.68-1.08%), minimal change from unadjusted (0.94%).

GRADE assessments: **Moderate certainty** for multiplex PCR diagnostic accuracy (downgraded: indirectness), hospital LOS reduction (downgraded: risk of bias), and age-stratified mortality

(downgraded: heterogeneity); **Low certainty** for epidemiological trends (downgraded: heterogeneity, indirectness), complication rates (downgraded: risk of bias, inconsistency), and treatment efficacy (downgraded: imprecision); **Very low certainty** for probiotic efficacy (downgraded: risk of bias, inconsistency, imprecision).

Discussion

Summary of Evidence

This comprehensive systematic review and meta-analysis consolidated evidence from 127 studies involving 2,847,392 adult patients across 42 countries. It represents the most extensive analysis to date of adult viral gastroenteritis epidemiology, diagnostic methodologies, therapeutic strategies, complications, and mortality outcomes during the pre-COVID period (2015-2019) and the post-COVID period (2022-2024). The principal findings reveal four key observations: first, the incidence of viral gastroenteritis has rebounded to levels exceeding those prior to the pandemic, with a 96% increase in norovirus outbreaks during the 2024-2025 season compared to the previous year; second, the widespread implementation of multiplex polymerase chain reaction panels has significantly enhanced diagnostic accuracy and clinical outcomes; third, elderly populations bear a disproportionately higher mortality burden, with risk ratios exceeding 21-fold when compared to younger adults; and fourth, epidemiological patterns specific to Türkiye generally mirror global trends while demonstrating distinct regional variations in pathogen distribution and healthcare utilization.

Comparison with Existing Literature

Our findings expand upon and contextualize previous analyses that have mainly concentrated on pediatric populations or individual pathogens. The Global Burden of Disease Study 2019 estimated that there are between 1.5 and 2.5 million deaths annually due to diarrheal diseases worldwide, with acute gastroenteritis ranking among the leading causes of infectious disease-related mortality [15]. Our data indicate that adult viral gastroenteritis significantly contributes to this burden, especially within elderly institutionalized populations residing in long-term care facilities, where case fatality rates range from 0.4% to 1.8%. These findings are consistent with epidemiological analyses conducted by Hall et al. and Ahmed et al., which identified norovirus as the primary causative agent of acute gastroenteritis across all age groups in high-income contexts [16,17].

The observed post-pandemic resurgence of viral gastroenteritis pathogens strongly supports the "immunity debt" hypothesis initially proposed by Cohen et al. and subsequently elaborated by Messacar et al [18,19]. This phenomenon, characterized by reduced population-level immunity following prolonged periods of decreased pathogen exposure during non-pharmaceutical intervention implementation, has been documented across multiple respiratory and enteric pathogens. Our finding of a disproportionate 100% increase in adenovirus F40/41 detection rates post-pandemic is consistent with pediatric surveillance data from multiple countries and suggests that certain pathogens may experience more pronounced resurgence dynamics. The mathematical modeling studies by Lappe et al. predicted such resurgence patterns, and our empirical data provide confirmatory evidence across diverse geographic settings [20,21].

The notable transition in norovirus genotype distribution, characterized by the decline of GII.4 Sydney from 68.4% to 42.8% of isolates and the concurrent rise of GII.17 from 8.2% to 32.6%, signifies a substantial epidemiological shift. This genotype replacement phenomenon has been previously documented during norovirus pandemic seasons and bears significant implications for vaccine development efforts, as current candidates primarily target GII.4 variants [22]. The emergence of GII.17 as the predominant strain in several Asian countries, now also observed in Türkiye and European regions, emphasizes the necessity for the development of broadly protective vaccine formulations.

Clinical and Public Health Implications

The clinical benefits associated with the implementation of multiplex PCR, as observed in our analysis, corroborate and expand upon the pioneering studies conducted by Beal et al. and Axelrad et al. [8,23]. The reduction of 60% in hospital length of stay (mean difference: -4.5 days), a 50% decrease in time to achieve optimal antimicrobial therapy, and a 312% increase in appropriate antibiotic discontinuation signify significant advancements in patient outcomes and antimicrobial stewardship. These findings hold immediate translational significance, endorsing the recommendation that multiplex molecular panels ought to be integrated as standard of care for hospitalized adults suffering from acute gastroenteritis, especially in environments where empiric antibiotic prescribing remains widespread.

The significantly increased mortality risk observed among elderly adults—with adjusted risk ratios of 8.4 for ages 65-74 years, 15.2 for ages 75-84 years, and 21.8 for those aged 85 years and above, in comparison to adults aged 18-64 years—serves to confirm and quantify the disproportionate burden experienced by older populations, as initially detailed by Cardemil et al. [24]. The analysis of the Veterans Health Administration cohort, which demonstrated elevated three-day mortality following norovirus infection (adjusted RR: 2.14, 95% CI: 1.10-4.14) [16], indicates an acute physiological insult that may trigger cardiovascular events or worsen existing comorbidities. These findings advocate for the implementation of enhanced surveillance protocols in long-term care facilities, lower thresholds for hospitalization among elderly patients, and expedited development of norovirus vaccines proven effective in older adult populations.

Türkiye-Specific Considerations

The 18 Turkish studies contributing 124,856 patients to this analysis represent the most comprehensive dataset from a middle-income country within the viral gastroenteritis literature. Several

notable features warrant attention. The earlier post-pandemic resurgence observed in Türkiye (Q3 2021 versus Q1 2022 in most European countries) likely reflects an earlier relaxation of non-pharmaceutical interventions and the resumption of international tourism, which exceeds 50 million annual visitors. The higher proportion of healthcare facility-associated outbreaks (42.3% versus 15-20% globally) contrasted with lower long-term care facility involvement (28.4% versus 60-65% globally) reflects Türkiye's demographic structure and lower institutionalization rates among elderly populations. The ninefold increase in multiplex PCR utilization from 2.1% to 18.6% demonstrates rapid diagnostic modernization, although regional disparities persist, with Eastern Anatolia and Southeastern regions having limited access to molecular diagnostics. The elevated empiric antibiotic prescribing rate of 32.8% compared to the global average of 24.2% highlights an important opportunity for antimicrobial stewardship [3,25].

Strengths and Limitations

This analysis has several methodological strengths: comprehensive multi-database searching including regional Turkish sources; large combined sample size that improves statistical accuracy; strict adherence to PRISMA 2020 guidelines; pre-specified subgroup and sensitivity analyses; and inclusion of Türkiye-specific data addressing an important gap in middle-income country representation. However, there are also notable limitations. Significant statistical heterogeneity (I^2: 28.4-88.4%) was found across most outcomes, indicating real differences in populations, settings, diagnostic methods, and outcome definitions among the included studies. The majority of evidence coming from high-income North American and European settings may limit its applicability to resource-limited contexts. The predominance of data from high-income North American and European settings (62.2% of included studies, representing 78.4% of the total pooled patient population) significantly limits the generalizability of our findings to resource-limited contexts where the burden of diarrheal disease is proportionally greater. Notably, Africa contributed only 3 studies (2.4%) and Southeast Asia was markedly underrepresented despite these regions bearing a substantial proportion of the global diarrheal disease burden—the Global Burden of Disease Study 2019 estimated that sub-Saharan Africa and South Asia together account for approximately 60% of global diarrheal mortality. This geographic imbalance introduces several potential biases that may substantially underestimate the true global burden of adult viral gastroenteritis and overlook critical region-specific factors. First, epidemiological patterns including circulating viral genotypes, seasonal transmission dynamics, and co-infection rates with other enteric pathogens may differ substantially in tropical and resource-limited settings. Second, diagnostic challenges related to limited laboratory infrastructure, reliance on clinical diagnosis without pathogen confirmation, and variable access to molecular testing platforms likely result in significant underascertainment of viral gastroenteritis cases in LMICs. Third, treatment practices constrained by resource availability—including limited access to intravenous fluids, antiemetics, and intensive care facilities—may influence clinical outcomes in ways not captured by predominantly high-income country data. Fourth, population-level factors unique to low-income settings, including younger age structure, higher prevalence of malnutrition and micronutrient deficiencies, endemic HIV/AIDS, co-existing parasitic infections, and variable access to oral rehydration therapy, may fundamentally alter disease severity, complication rates, and mortality determinants. Fifth, healthcare system characteristics including delayed presentation due to geographic barriers, limited healthcare worker training in fluid resuscitation, and absence of systematic outbreak surveillance may influence both the detection and outcomes of viral gastroenteritis in these settings. Collectively, these factors suggest that our pooled estimates, derived predominantly from well-resourced healthcare systems with advanced diagnostic capabilities and comprehensive supportive care, may not accurately reflect the burden and outcomes of adult viral gastroenteritis in the populations most affected by diarrheal diseases globally [26].The observational design of the included studies prevents causal conclusions and may introduce confounding factors. Differences in diagnostic criteria and reliance on passive surveillance systems for outbreak data could lead to underreporting. Lastly, although funnel plot asymmetry and Egger's test indicated potential publication bias for mortality outcomes, the trim-and-fill analysis suggested a minimal effect on the pooled estimates [27]. The substantial statistical heterogeneity observed across most outcomes (I^2: 28.4-88.4%) warrants careful interpretation of pooled estimates. However, this heterogeneity should not be viewed solely as a limitation but rather as an inherent characteristic of global infectious disease epidemiology that provides valuable insights into factors influencing VGE outcomes. The significant heterogeneity identified through subgroup analyses—demonstrating differential outcomes by geographic region, healthcare setting, age group, and diagnostic methodology—highlights the context-dependent nature of VGE burden and the importance of tailoring prevention and management strategies to local circumstances. The random-effects model employed in our analyses appropriately accounts for this between-study variability, and the consistency of findings across multiple sensitivity analyses (exclusion of high-risk-of-bias studies, leave-one-out analysis, fixed-effect models, outlier removal) supports the robustness of our principal conclusions

Future Research Directions

Several priority areas for future investigation emerge from this analysis. First, standardization of outcome definitions and diagnostic criteria would enhance comparability across surveillance systems and research studies. Second, and most urgently, addressing the geographic evidence gap through investment in research infrastructure and surveillance capacity in underrepresented low- and middle-income country settings represents a critical priority for the field. Prospective surveillance

studies in sub-Saharan Africa, Southeast Asia, and South Asia are needed to characterize the regional epidemiology, pathogen distribution, and disease burden of adult viral gastroenteritis in populations bearing the greatest burden of diarrheal diseases globally. Such studies should incorporate molecular diagnostics where feasible to enable pathogen identification and genotyping, thereby contributing to global understanding of viral strain circulation and evolution. Standardized case definitions aligned with international surveillance frameworks should be employed to facilitate meaningful cross-regional comparisons. Implementation research examining the feasibility, cost-effectiveness, and clinical utility of simplified diagnostic algorithms and treatment protocols specifically adapted for resource-limited settings would provide actionable evidence to inform clinical practice guidelines in these underserved populations. International research collaborations between established surveillance networks (such as the Global Enteric Multicenter Study and the Malnutrition and Enteric Disease Study) and emerging research institutions in underrepresented regions, supported by capacity-building initiatives from global health organizations including the World Health Organization and the Bill & Melinda Gates Foundation, should be actively prioritized and funded [26].Third, economic evaluations comparing multiplex PCR implementation strategies would inform resource allocation decisions in diverse healthcare systems. Fourth, long-term follow-up studies examining post-infectious sequelae, including post-infectious irritable bowel syndrome, would quantify the chronic disease burden attributable to viral gastroenteritis. Fifth, clinical trials evaluating targeted interventions for elderly populations—including enhanced infection control protocols, antiviral agents, and candidate vaccines—represent critical unmet needs given the disproportionate mortality burden in this vulnerable population.

Conclusion

This systematic review of 127 studies with 3 million patients shows post-COVID viral gastroenteritis has surged, with norovirus outbreaks up 96% and incidence above pre-pandemic levels. Multiplex PCR panels have improved outcomes, cutting hospital stays by 60% and aiding antibiotic stewardship. Elderly groups are most at risk, with mortality risk ratios over 21 times higher in those 85+, stressing prevention and vaccine needs. Türkiye's data reflects global patterns but suggests better molecular diagnostics and antimicrobial strategies. These results highlight the need for improved surveillance, rapid diagnostics, and norovirus vaccine development to protect vulnerable elderly populations. Finally, the marked geographic concentration of available evidence in high-income settings—with sub-Saharan Africa and Southeast Asia contributing less than 5% of included studies despite bearing the majority of global diarrheal disease burden—underscores the critical and urgent need for expanded research infrastructure, surveillance capacity, and funding prioritization in low- and middle-income countries to achieve a truly comprehensive global understanding of adult viral gastroenteritis epidemiology and outcomes.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical Approval
Ethics committee approval was not required because this study was based solely on previously published and publicly available data and did not involve human subjects or primary data collection.

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