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Global burden of enteric infections related foodborne diseases, 1990–2021: findings from the Global Burden of Disease Study 2021

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ABSTRACT

Background: Understanding the global burden of enteric infections is crucial for prioritizing control strategies for foodborne and waterborne diseases. This study aimed to assess the global burden of enteric infections in 2021 and identify risk factors from One Health aspects.

Methods: Leveraging the Global Burden of Disease (GBD) 2021 database, the incidence, disability-adjusted life years (DALYs), and deaths of enteric infections and the subtypes were estimated, including diarrheal diseases, typhoid and paratyphoid fever, invasive non-typhoidal *Salmonella* (iNTS) infections, and other intestinal infectious diseases. The estimates were quantified by absolute number, age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR) and age-standardized DALY rate with 95% uncertainty intervals (*UI*s). Thirteen pathogens and three risk factors associated with diarrheal diseases were analyzed.

Results: In 2021, the global age-standardized DALY rate of enteric infections was 1020.15 per 100,000 popultion (95% *UI*: 822.70–1259.39 per 100,000 population) with an estimated annual percentage change (EAPC) of −4.11% (95% confidence interval: −4.31% to −3.90%) in 1990–2021. A larger burden was observed in regions with lower Socio-demographic index (SDI) levels. Diarrheal disease was the most serious subtype with Western Sub-Saharan Africa exhibiting the highest age-standardized DALY rate (2769.81 per 100,000 population, 95% *UI*: 1976.80–3674.41 per 100,000 population). Children under 5 and adults over 65 years suffered more from diarrheal diseases with the former experiencing the highest global age-standardized DALY rate (9382.46 per 100,000 population, 95% *UI*: 6771.76–13,075.12 per 100,000 population). Rotavirus remained the leading cause of diarrheal diseases despite a cross-year decline in the observed age-standardized DALY rate. Unsafe water, sanitation, and handwashing contributed most to the disease burden.

Conclusion: The reduced burden of enteric infections suggested the effectiveness of previous control strategies; however, more efforts should be made in vulnerable regions and populations through a One Health approach.

Abbreviations: ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASRs, age-standardized rates; *CIs*, confidence intervals; DALYs, disability-adjusted life years; EAPC, estimated annual percentage change; GBD, Global Burden of Disease; HALE, Healthy Life Expectancy; ICD, International Classification of Diseases; iNTS, invasive non-typhoidal *Salmonella*; MDGs, Millennium Development Goals; SDGs, Sustainable Development Goals; SDI, Socio-demographic index; *UIs*, uncertainty intervals; UN, United Nation.

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1. Background

Enteric infections are classic foodborne and waterborne diseases caused by bacteria, viruses, parasites, or chemical substances through the fecal-oral route [1,2]. The subtypes of enteric infections include diarrheal diseases, typhoid and paratyphoid fever, invasive non-typhoidal *Salmonella* (iNTS) infections, and others. Common pathogens include norovirus, rotavirus, *Salmonella*, *S. enterica* serovar Typhi, etc. Pathogens are usually infectious or toxic and can be transmitted through contaminated water or food, leading to infections in humans or animals [3]. Foodborne and waterborne diseases affect billions of people each year, placing a heavy burden on public health [4,5]. Unsafe water and poor sanitation infrastructure are common environmental factors that affect the disease burden.

In 2000, the Millennium Development Goals (MDGs) proposed by United Nation (UN) identified diarrheal disease control as a key priority for achieving MDG 4, which aimed to reduce child mortality [6]. In 2015, the UN proposed the Sustainable Development Goals (SDGs) with SDG 3 seeking to combat waterborne and other communicable diseases, SDG 4 ensuring inclusive and equitable quality education, and SDG 11 ensuring access for all to adequate, safe and affordable housing and basic services by 2030 [7]. World Health Organization has implemented measures to reduce the burden of enteric infections by promoting national policies and investment in diarrheal disease management [8]. However, enteric infections continue to pose a significant disease burden globally, and remain among the top 10 causes of death worldwide with 550 million people falling ill annually [9,10]. Typhoid fever, an enteric infection subtype, remains an important global public health concern [11] with 9 million cases and about 110,000 deaths annually [12]. Most cases of non-typhoidal salmonellosis disease are mild, but some are life-threatening [10]. To our knowledge, the global burden of enteric infections is only known until 2019; no details are available for 2021.

Environment is among the most important factors driving enteric infections. Mitigating the burden of enteric infections depends on holistic strategies targeting not only humans, but also environmental factors. However, how potential risk factors associated with the environment contribute to this burden remains unclear. The One Health concept emphasizes the overall health of humans, animals, and the environment, which is consistent with the idea of reducing the disease burden of enteric infections. Therefore, this study used comprehensive data from the Global Burden of Disease (GBD) 2021 study to provide an in-depth analysis of the multifaceted implications of enteric infections worldwide. This study quantified the incidence, mortality, and disability-adjusted life years (DALYs) of enteric infections on global, regional, and national scales, helping to identify vulnerable regions, prevailing etiologic factors, and risk factors. By tracing the updated GBD of enteric infections, this study was significant in assessing the effectiveness of policies adopted for managing enteric infections and could further inform possible interventions based on the One Health approach. This study may also contribute to identifying and addressing the root causes of enteric infections from a One Health perspective, which may be significant for achieving the SDGs.

2. Methods

2.1. Data source

GBD 2021 provides estimates of 371 diseases and injuries, and 88 risk factors in 204 countries and territories from 1990 to 2021 [13,14]. The studied data were obtained from the Institute for Health Metrics and Evaluation website (https://vizhub.healthdata.org/gbd-results/). The GBD 2021 provides estimates of the burden of enteric infections for four diseases: diarrheal diseases, typhoid and paratyphoid fever, iNTS infections, and other intestinal infectious diseases. The specific search strategies were GBD Estimate (cases of death or injury, risk factor, etiology), Measure (incidence, deaths, DALYs), Metric (rate, number), Cause (enteric infections, diarrheal diseases, typhoid and paratyphoid, iNTS, other intestinal infectious diseases), Location (global, all GBD super-regions, all GBD regions, different Socio-demographic index [SDI] regions, 204 countries and territories), Age (all ages, age-standardized, age groups from <5 years to 95+ years at a 5-year interval). The analysis of risk factors for enteric infections was based on the human-environment interface, considering unsafe environments and human behavioral correlates. GBD 2021 classified GBD risk factors into a four-level hierarchy. Due to data availability, data on risk factors related to diarrheal diseases were retrieved at level 2 from GBD 2021, including unsafe water, sanitation, and handwashing; child and maternal malnutrition; and air pollution.

SDI is a composite indicator of lag-distributed income per capita, average years of education, and fertility rates among females younger than 25 years [13]. SDI values range from 0 to 1; 0 indicates the lowest development level theoretically, and 1 indiactes the highest. The 204 countries and territories were grouped into five categories by SDI values for subgroup analysis: low (0.0000–0.4658), low-middle (0.4658–0.6188), middle (0.6188–0.7120), high-middle (0.7120–0.8103), and high (0.8103–1.0000) (Table S1).

2.2. Case definition

The burden of enteric infections was measured based on the incidence, deaths, and DALYs attributable to enteric infections and their subtypes caused by 13 different enteric pathogens. Enteric infections and subtypes were defined according to the International Classification of Diseases (ICD), 10th Revision (Table S2) [13]. The 13 pathogens were selected using the available etiologies related to diarrheal diseases in the GBD dataset. DALYs are the sum of years lived with disability and years of life lost. Previous studies have described the methodology used to estimate the number of deaths and DALYs in detail [13].

The GBD classifies the globe into seven super-regions and 21 subregions based on epidemiological similarity and geographic proximity (Table S3).

2.3. Data analysis

The measurements in this study included absolute numbers and rates of incidence, mortality, and DALYs, where the rates were age-standardized and presented as age-standardized incidence rate (ASIR), age-standardized mortality rate (ASMR), and age-standardized DALY rate (per 100,000 population). The absolute numbers and age-standardized rates (ASRs) of the disease burden metrics were extracted from the GBD 2021 database. Corresponding data were presented as estimates with 95% uncertainty intervals (*UIs*). The formula for calculating the ASRs (per 100,000 population) was as follows:

$$\mathrm{ASR} = \frac{\sum_{i=1}^{N} a_i w_i}{\sum_{i=1}^{N} w_i}$$

where a_i represents the age-specific rate for the i-th age group and w_i represents the number (or the weight) of people in the corresponding age group among the GBD standard population. N represents the number of age groups. The 95% *UI* was defined as the 2.5th and 97.5th values of the ordered 1000 draws.

The estimated annual percentage change (EAPC) was used to quantify changing trends from 1990 to 2021. A linear regression model was fitted based on the natural logarithm of ASR ($y = \alpha + \beta x + \varepsilon$), where y was equal to logarithmically transformed ASR. EAPC was then calculated as $100 \times (e^{\beta} - 1)$, and 95% confidence intervals (*CIs*) were obtained from the linear regression model [15]. A significant downward trend over the observed period was considered if the upper limit of the EAPC 95% *CI* was <0. Conversely, a significant increasing trend was considered if the lower limit of the EAPC 95% *CI* was >0. Non-significant change was considered when the 95% *CI* included 0 [16]. A significant difference between groups was considered when comparing two values if their *UI*s did not overlap and vice versa.

All statistical analysis and mapping were performed using **R** software (version 4.0.2).

3. Results

3.1. Global overview

The global burden of enteric infections has significantly decreased over the past three decades. In 2021, there were 4.45 billion (95% *UI*: 3.97–4.99 billion) incident cases of enteric infections reported with the ASIR of 5.77 per billion population (95% *UI*: 5.12–6.48 per billion population) (Table S4). The ASMR and age-standardized DALY rate of enteric infections were 17.83 per 100,000 population (95% *UI*: 13.38–23.50 per 100,000 population) and 1020.15 per 100,000 population (95% *UI*: 822.70–1259.39 per 100,000 population), respectively, with the EAPC of ASMR and age-standardized DALY rate reaching −4.13% (95% *CI*: −4.32% to −3.94%) and −4.11% (95% *CI*: −4.31% to −3.90%), respectively, between 1990 and 2021 (Table 1). The global age-standardized DALY rate in 2021 were 834.18 per 100,000 population (95% *UI*: 663.40–1041.11 per 100,000 population), 115.26 per 100,000 population (95% *UI*: 59.32–198.47 per 100,000 population), 69.14 per 100,000 population (95% *UI*: 39.70–111.21 per 100,000 population), and 1.57 per 100,000 population (95% *UI*: 1.13–2.10 per 100,000 population) for diarrheal diseases, typhoid and paratyphoid fever, iNTS infections, and other intestinal infectious diseases, respectively (Table S5−S8). The absolute number of deaths and DALYs for enteric infections and their four subtypes were shown in Table S9−S13. Among the four subtypes of enteric infections, diarrheal diseases exhibited the highest disease burden.

3.2. The regional and national distribution of DALYs

Regions and countries exhibited variable patterns in the burden of enteric infections. In 2021, Western Sub-Saharan Africa was the most affected region with an age-standardized DALY rate of 3383.88 per 100,000 population (95% *UI*: 2464.90–4393.17 per 100,000 population), and Chad showed the largest burden at the national level with an age-standardized DALY rate of 7791.23 per 100,000 population (95% *UI*: 5423.71–11,385.15 per 100,000 population) (Table 1, Fig. 1). Regions or counties with small land areas were shown as submaps in Fig. 1. The regional distribution of the age-standardized DALY rates for the four subtypes was shown in Fig. S1−S4. For diarrheal diseases, Western Sub-Saharan Africa continued to have the highest age-standardized DALY rate (2769.81 per 100,000 population, 95% *UI*: 1976.80–3674.41 per 100,000 population) (Fig. S1), and Chad also showed the highest age-standardized DALY rate (7341.22 per 100,000 population, 95% *UI*: 5070.03–10,968.21 per 100,000 population). In addition, East Asia experienced the greatest decline in the age-standardized DALY rate for diarrheal diseases over 1990–2021 with EAPC reaching −10.90% (95% *CI*: −11.42% to −10.38%) (Table S5). Moreover, other intestinal infections showed the least burden compared to other subtypes worldwide (Fig. S4).

3.3. Temporal trends of enteric infections by SDI levels

The age-standardized DALY rates for enteric infections and subtypes of diarrheal diseases, typhoid and paratyphoid fever, and other intestinal infectious diseases showed downward trends across different SDI regions between 1990 and 2021. Diarrheal diseases exhibited a substantial decline in age-standardized DALY rates among the four enteric infections subtypes. Low SDI regions showed notable declines with the age-standardized DALY rate decreasing from 9231.04 per 100,000 population (95% *UI*: 7207.31–11,730.12 per 100,000 population) in 1990 to 2605.84 per 100,000 population (95% *UI*: 1986.90–3395.52 per 100,000 population) in 2021. Meanwhile, the age-standardized DALY rate for iNTS infections in low SDI regions peaked at 479.25 per 100,000 population (95% *UI*: 273.00–742.91 per 100,000 population) in 2005 before decreasing to 234.06 per 100,000 population (95% *UI*: 135.30–376.15 per 100,000 population) by 2021 (Fig. 2).

3.4. Sex differences by age groups

Global populations in different age groups and sexes exhibited varied disease burden patterns for enteric infections and the four subtypes in 2021 (Fig. 3). Children under five showed the highest burdens with the age-standardized DALY rate of 9382.46 per 100,000 population (95% *UI*: 6771.76–13,075.12 per 100,000 population) in both sexes, 6054.32 per 100,000 population (95% *UI*: 4216.04–8501.64 per 100,000 population) in males and 5377.25 per 100,000 population (95% *UI*: 4010.62–7082.82 per 100,000 population) in females. The age-standardized DALY rates for enteric infections and diarrheal diseases first showed decreasing trends and then showed increasing trends according to age group. Adults aged 60 years or over also showed a pronounced disease burden. Higher age-standardized DALY rates and ASMR of enteric infections were observed among males than among females across age groups, although no statistical difference was detected.

3.5. Relationship between disease and SDI

The burden of enteric infections varied greatly with SDI at regional and national levels (Fig. S5−S8). The age-standardized DALY rate and ASMR for diarrheal diseases, iNTS, and other intestinal infections were negatively associated with SDI levels while almost reached zero in the high SDI regions. There was an approximately linear decrease in both the ASMR and age-standardized DALY rate for iNTS when SDI values were less than 0.5. However, the ASMR and age-standardized DALY rate for typhoid and paratyphoid fever tended to increase and then decrease with increasing SDI.

3.6. Pathogens and risk factors for diarrheal diseases

Thirteen pathogens that caused diarrheal diseases were analyzed in this study (Fig. 4). Among them, rotavirus was the most prominent pathogen for age-standardized DALY rate of diarrheal diseases worldwide in 2021 (Fig. S9), reaching an attributable proportion of 0.24% (95% *UI*: 0.20%–0.30%). Children under five were the most affected by these 13 pathogens. In high-income regions, however, there was an increasing trend of age-standardized DALY rate for diarrheal diseases attributable to *Clostridium difficile* from 0.06% (95% *UI*: 0.04%–0.08%) in 1990 to 0.20% (95% *UI*: 0.16%–0.24 %) in 2021.

Three main risk factors that may contribute to the burden of diarrheal diseases—unsafe water, sanitation, and handwashing; child and maternal malnutrition; and air pollution— were shown in Figs. 5 and 6. The attributable proportion of risk factors were obtained by the GBD 2021 through attribution analysis and directly reflected the burden of disease due to risk factors [13]. The disease burden associated with each risk factor exhibited a downward trend from 1990 to 2021. The disease burden attributed to unsafe water, sanitation, and handwashing account for the largest proportion in all SDI regions.

4. Discussion

This study found an overall downward trend in the burden of enteric infections from 1990 to 2021. Diarrheal diseases were the most serious subtype of enteric infections worldwide. Children under five were the most affected by enteric infections. From 1990 to 2021, the burden of diarrheal diseases caused by most pathogens and three risk factors showed a decreasing trend. Rotavirus was the leading pathogen, and

Table 1
Age-standardized mortality rates and age-standardized DALY rates of enteric infections in 1990 and 2021, and estimated annual percentage changes by GBD regions.

Region	Mortality			DALYs		
	ASMR, per 100,000 population, 1990 (95% *UI*)	ASMR, per 100,000 population, 2021 (95% *UI*)	EAPC, % (95% *CI*)	Age-standardized DALY rate, per 100,000 population, 1990 (95% *UI*)	Age-standardized DALY rate, per 100,000 population, 2021 (95% *UI*)	EAPC, % (95% *CI*)
Global	65.42 (51.24–84.57)	17.83 (13.38–23.50)	−4.13 (−4.32–−3.94)	3704.93 (3017.57–4378.27)	1020.15 (822.70–1259.39)	−4.11 (−4.31–−3.90)
High SDI	0.93 (0.81–1.07)	1.16 (1.00–1.26)	1.97 (1.17–2.78)	82.61 (66.28–101.35)	57.86 (47.68–71.48)	−0.43 (−0.81–−0.04)
High-middle SDI	5.75 (4.52–6.94)	1.30 (1.01–1.59)	−4.87 (−5.20–−4.54)	457.68 (379.32–539.82)	84.66 (70.00–102.51)	−5.49 (−5.67–−5.32)
Middle SDI	44.62 (31.16–60.70)	8.76 (5.79–12.13)	−5.17 (−5.25–−5.09)	2165.20 (1710.63–2608.81)	426.35 (340.12–529.48)	−5.18 (−5.25–−5.11)
Low-middle SDI	195.73 (146.35–270.28)	42.10 (27.89–63.93)	−4.90 (−5.04–−4.76)	7736.82 (6275.42–9694.76)	1482.56 (1168.18–1949.54)	−5.22 (−5.37–−5.08)
Low SDI	238.69 (176.86–322.28)	75.25 (50.89–110.13)	−3.66 (−3.90–−3.43)	10,086.49 (8032.21–12,568.07)	2999.43 (2315.53–3859.13)	−3.85 (−4.09–−3.60)
Central Europe, Eastern Europe, and Central Asia	5.13 (4.71–5.62)	1.32 (1.11–1.61)	−5.83 (−6.53–−5.12)	474.73 (434.24–520.05)	101.67 (81.94–125.73)	−6.23 (−6.75–−5.71)
Central Asia	15.57 (14.13–17.31)	1.96 (1.46–2.62)	−7.80 (−8.22–−7.38)	1387.58 (1256.32–1542.30)	181.19 (136.74–239.60)	−7.61 (−8.01–−7.22)
Central Europe	1.17 (1.07–1.29)	1.38 (1.23–1.52)	1.21 (−0.46–2.91)	95.89 (86.50–105.90)	53.61 (47.20–60.41)	−1.58 (−2.79–−0.35)
Eastern Europe	1.19 (1.14–1.24)	0.26 (0.24–0.27)	−6.64 (−7.37–−5.90)	137.88 (122.02–157.69)	38.44 (29.69–49.29)	−4.81 (−5.18–−4.43)
High-income	0.75 (0.69–0.80)	1.17 (1.00–1.27)	2.76 (1.92–3.61)	72.05 (58.00–90.22)	55.31 (45.55–68.51)	−0.08 (−0.58–0.43)
Australasia	0.70 (0.63–0.76)	0.50 (0.42–0.55)	0.89 (−0.30–2.09)	48.95 (39.08–62.29)	19.75 (16.68–23.93)	−2.59 (−3.05–−2.14)
High-income Asia Pacific	1.09 (0.89–1.28)	0.80 (0.64–1.00)	−0.33 (−0.63–−0.04)	84.52 (65.63–108.32)	85.92 (63.03–115.97)	0.55 (0.26–0.84)
High-income North America	0.31 (0.28–0.32)	1.49 (1.30–1.60)	6.73 (5.00–8.49)	31.81 (25.32–39.61)	32.31 (29.91–34.20)	1.58 (0.72–2.44)
Southern Latin America	3.57 (3.37–3.75)	1.53 (1.36–1.69)	−1.89 (−2.41–−1.36)	261.95 (233.82–292.40)	65.46 (56.41–77.33)	−3.56 (−3.98–−3.15)
Western Europe	0.57 (0.51–0.61)	1.12 (0.95–1.23)	3.33 (2.41–4.25)	64.77 (47.21–86.15)	68.24 (52.83–88.15)	0.71 (0.08–1.35)
Latin America and Caribbean	31.41 (29.34–33.45)	4.75 (4.01–5.66)	−5.95 (−6.41–−5.49)	2083.28 (1939.92–2227.08)	267.19 (217.02–325.39)	−6.50 (−6.86–−6.14)
Andean Latin America	25.00 (20.54–29.79)	2.92 (2.03–4.47)	−7.20 (−7.51–−6.89)	1740.97 (1495.65–2017.34)	172.70 (129.89–229.98)	−7.74 (−8.01–−7.48)
Caribbean	38.17 (32.33–44.70)	14.02 (9.89–18.88)	−3.04 (−3.49–−2.59)	2949.73 (2473.35–3457.24)	1090.49 (769.64–1461.56)	−2.93 (−3.40–−2.47)
Central Latin America	36.58 (34.73–38.60)	5.29 (4.52–6.22)	−5.98 (−6.60–−5.37)	2131.81 (2007.71–2281.90)	265.96 (220.20–324.16)	−6.49 (−7.00–−5.98)
Tropical Latin America	27.86 (25.18–30.74)	2.71 (2.37–2.92)	−7.50 (−7.93–−7.07)	2013.90 (1754.51–2276.45)	116.69 (102.98–133.14)	−9.22 (−9.48–−8.96)
North Africa and Middle East	23.04 (17.70–28.30)	3.53 (2.62–4.75)	−6.10 (−6.22–−5.99)	1828.07 (1439.57–2272.01)	280.40 (216.48–367.29)	−6.06 (−6.17–−5.95)
North Africa and Middle East	23.04 (17.70–28.30)	3.53 (2.62–4.75)	−6.10 (−6.22–−5.99)	1828.07 (1439.57–2272.01)	280.40 (216.48–367.29)	−6.06 (−6.17–−5.95)
South Asia	244.28 (182.77–341.71)	52.25 (34.34–81.39)	−4.93 (−5.04–−4.82)	8614.11 (6967.05–10,994.24)	1688.36 (1282.69–2324.84)	−5.18 (−5.29–−5.08)
South Asia	244.28 (182.77–341.71)	52.25 (34.34–81.39)	−4.93 (−5.04–−4.82)	8614.11 (6967.05–10,994.24)	1688.36 (1282.69–2324.84)	−5.18 (−5.29–−5.08)
Southeast Asia, East Asia, and Oceania	36.68 (23.83–52.96)	5.03 (3.36–6.47)	−6.38 (−6.55–−6.22)	1901.40 (1406.36–2403.57)	293.62 (232.39–368.81)	−6.13 (−6.29–−5.98)
East Asia	9.34 (6.77–11.71)	0.44 (0.33–0.63)	−10.39 (−10.83–−9.95)	704.87 (543.19–866.71)	36.88 (29.99–45.96)	−10.17 (−10.65–−9.70)
Oceania	87.31 (55.51–118.97)	43.48 (27.78–62.25)	−1.93 (−2.10–−1.75)	3516.23 (2461.72–4697.44)	1780.07 (1253.70–2384.70)	−1.87 (−2.02–−1.73)
Southeast Asia	103.91 (62.24–159.88)	16.32 (9.52–21.72)	−5.76 (−5.97–−5.56)	4606.59 (3317.73–6186.11)	702.82 (539.90–881.87)	−5.89 (−6.08–−5.70)
Sub-Saharan Africa	178.00 (123.75–240.41)	59.64 (39.06–81.11)	−3.53 (−3.81–−3.24)	8936.21 (6721.28–11,019.91)	2783.68 (2083.85–3604.93)	−3.70 (−4.01–−3.40)
Central Sub-Saharan Africa	160.15 (112.14–214.78)	43.08 (25.65–67.35)	−4.23 (−4.96–−3.49)	7871.80 (5827.77–9703.13)	1728.05 (1182.63–2452.90)	−4.83 (−5.62–−4.04)
Eastern Sub-Saharan Africa	189.33 (120.94–269.77)	62.72 (37.23–84.34)	−3.64 (−3.78–−3.50)	8687.05 (6378.77–11,427.40)	2523.08 (1853.83–3295.26)	−4.02 (−4.13–−3.91)
Southern Sub-Saharan Africa	83.73 (61.41–117.61)	40.58 (26.73–58.19)	−2.08 (−2.40–−1.75)	4549.14 (3897.50–5421.14)	1941.05 (1555.22–2486.17)	−2.51 (−2.88–−2.15)
Western Sub-Saharan Africa	202.98 (138.58–273.15)	65.53 (45.98–88.84)	−3.64 (−3.96–−3.31)	10,608.59 (7794.83–12,909.47)	3383.88 (2464.90–4393.17)	−3.60 (−3.95–−3.24)

Abbreviations: ASMR, age-standardized mortality rate; *CI*, confidence interval; DALYs, disability-adjusted life years; EAPC, estimated annual percentage change; GBD, global burden of disease; SDI, Socio-demographic index; *UI*, uncertainty interval.

unsafe water, sanitation, and handwashing were the leading risk factors. At regional level, most regions experienced a decreasing disease burden of enteric infections from 1990 to 2021. This study observed that, in 2021, the highest disease burdens for the four disease subtypes were predominantly distributed in low SDI regions, such as Western Sub-Saharan Africa.

Diarrhea-associated deaths and DALYs were higher among children under five than those in any other age groups, followed by the elderly, which is in line with other reports [17–19]. Globally, diarrheal diseases were the leading cause of death among adolescents in 2019, ranking the first among adolescent girls and second among adolescent boys [20]. Numerous factors may be linked to diarrheal diseases in children under five, for example, child's age [21], mother's educational status [22], and travel time to water sources [23]. Vaccination may be an effective measure to reduce the burden of diarrheal diseases in adolescents with benefits extending beyond early childhood and into adolescence [20]. Diarrhea-associated deaths were also elevated in populations aged 60 and above [24]. This mechanism may be attributed to aging, which may lead to decreased nutritional conditions, immune responses, and kidney function. Enteric infections may be triggered or worsened by concurrent illnesses in older adults [25]. Improving health literacy played an important role in addressing the burden of diarrheal diseases [5]. Additional educational initiatives and health promotion tactics should be implemented for both children and the elderly. Moreover, strengthening health-care services may be important to reduce the burden of diarrheal diseases in the elderly.

The burden of enteric infections was generally negatively correlated with SDI levels worldwide, as reported in previous studies [24,26,27]. Low SDI regions and countries were constrained by their economic levels and invested relatively little in sanitation [28], which could present significant hurdles in effectively tackling enteric infections [29]. Previous studies have found that poor sanitation posed a significant enteric infections challenge in low- and middle-income countries, such as East African countries [30,31]. In addition, poverty limited access to basic social services in these countries or regions, resulting in problems such as lack of timely access to health care. The SDGs propose to eradicate extreme poverty for all people and achieve substantial coverage of the poor through the implementation of social protection systems and

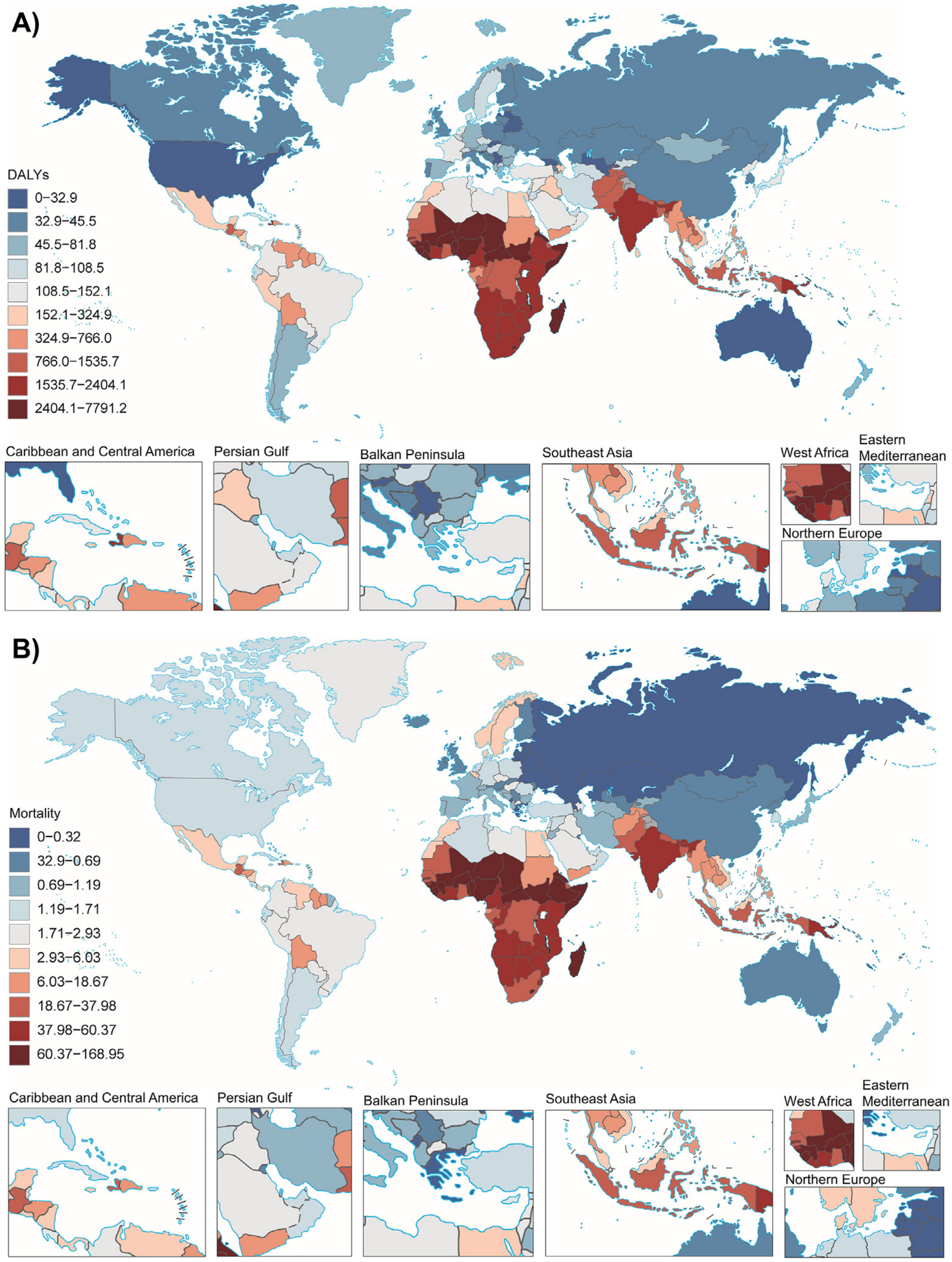

Fig. 1. Global burden of diseases due to enteric infections in 2021. A: Age-standardized DALY rates in 2021. B: Age-standardized mortality rates in 2021. The burden of disease in Caribbean and Central America, Persian Gulf, Balkan Peninsula, Southeast Asia, West Africa, Eastern Mediterranean, and Northern Europe were shown in small maps. Abbreviation: DALY, disability adjusted life year.

measures by 2030 [32], which might help reduce the disease burden of poverty-induced enteric infections. Moreover, socio-demographic development policies in low- and middle-SDI regions may contribute to reducing mortality from enteric infections [33].

The safe use of water remains a significant global challenge. A lack of access to safe water and sanitation services could lead to an exponential increase in diseases, especially waterborne diseases [34]. However, only 74% of the population had access to basic hand-washing facilities globally, 70% of which were in low- and middle-income countries [31]. A recent study indicated that unsafe drinking water, sanitation, and hygiene were responsible for 69% of diarrheal diseases, accounting for over one million deaths and approximately 55 million DALYs. The One Health approach indicates that focusing on environmental risk factors helps to advance disease prevention and control. Maintaining a clean and hygienic environment could effectively reduce the growth of pathogens, which helps to interrupt the spread of diseases at their source. Therefore, ensuring water security by improving the environment should be considered, particularly in low-income countries [35]. Public health interventions, such as chlorination of drinking water [36] and investment in environmental improvements [37], could reduce the burden of disease at the human–environment interface.

The global threat of enteric infections, especially diarrheal diseases, which often originated at the human-animal-environment interface, has caught health systems off guard [38]. Given the projections that the future emergence of pathogens may predominantly occur within lower SDI regions, there is an immediate need to prepare a One Health approach capable of combating this threat [39,40]. By 2023, SDGs 4 and

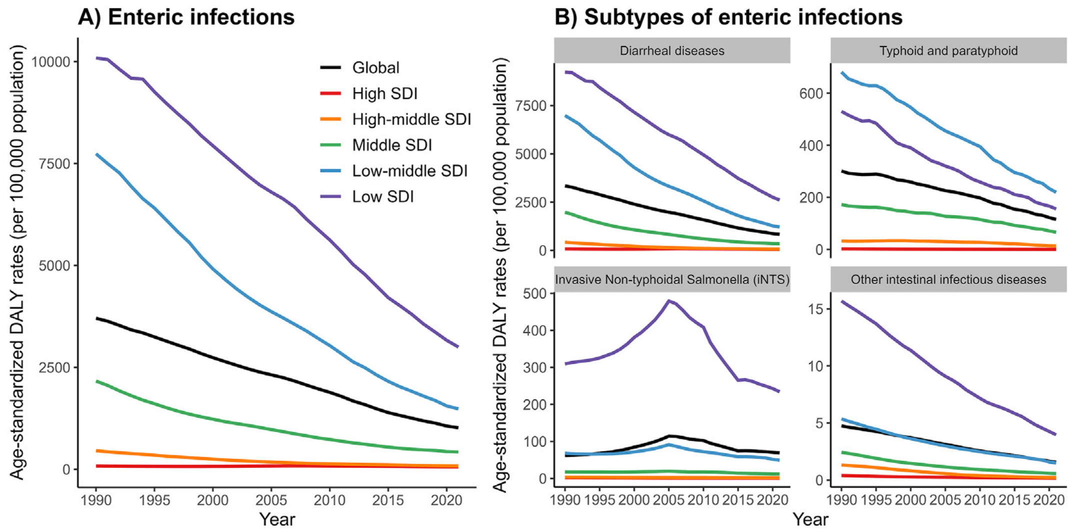

Fig. 2. Temporal trends in the age-standardized DALY rates due to enteric infections across different SDI regions from 1990 to 2021. A: Temporal trends of enteric infections. B: Temporal trends in enteric infections subtypes. Abbreviations: DALY, disability adjusted life year; SDI, Socio-demographic index.

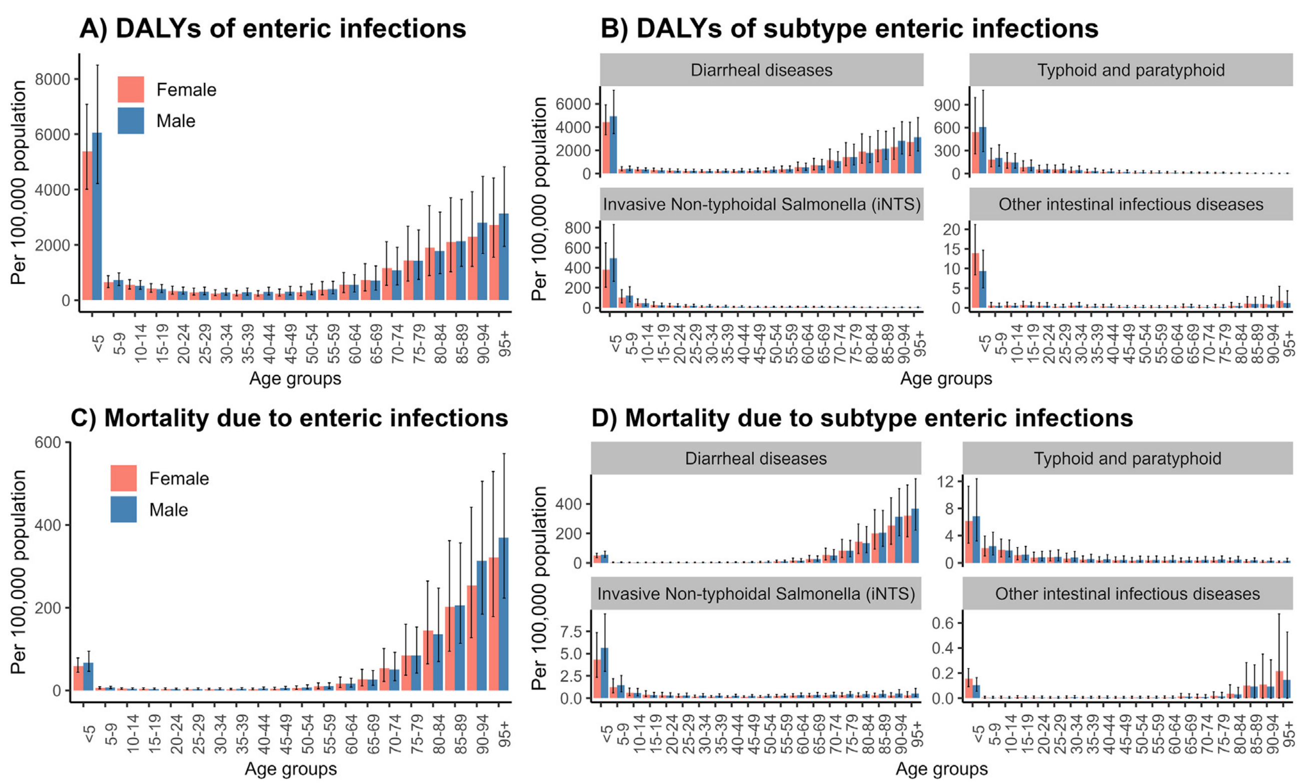

Fig. 3. Age-standardized DALY rate and age-standardized mortality rate due to enteric infections in the global populations of different age groups in 2021. A: DALYs of enteric infections (per 100,000 population). B: DALYs of subtype enteric infections (per 100,000 population). C: Mortality due to enteric infections (per 100,000 population). D: Mortality due to subtype enteric infections (per 100,000 population). Abbreviation: DALY, disability adjusted life year.

11 were at a moderate distant from the targets for completion; however, SDG 3 was still far from the expected progress and had even regressed compared to 2020. This study contributes to the achievement of SDGs by analyzing the vulnerability and providing targeted interventions. Investment in sanitation infrastructure, which includes providing safe drinking water, improving hygiene conditions, and promoting basic hand-washing facilities, is crucial for reducing enteric infections [41,42]. Moreover, reducing pathogen breeding by improving environmental conditions, such as sewage treatment, could further lower the risk of disease transmission [36]. Implementing comprehensive measures with a One Health approach can be more effective in addressing the challenges of enteric infections and working toward healthier, more sustainable communities on a global scale, especially in lower SDI regions.

This study has several limitations. First, GBD data may not be updated in real time, which means that they may not reflect the most recent health data and trends. Meanwhile, mild symptoms of enteric infections might not be recorded, which could lead to an underestimation of the incidence or prevalence [43]. Second, GBD relies on various available sources, such

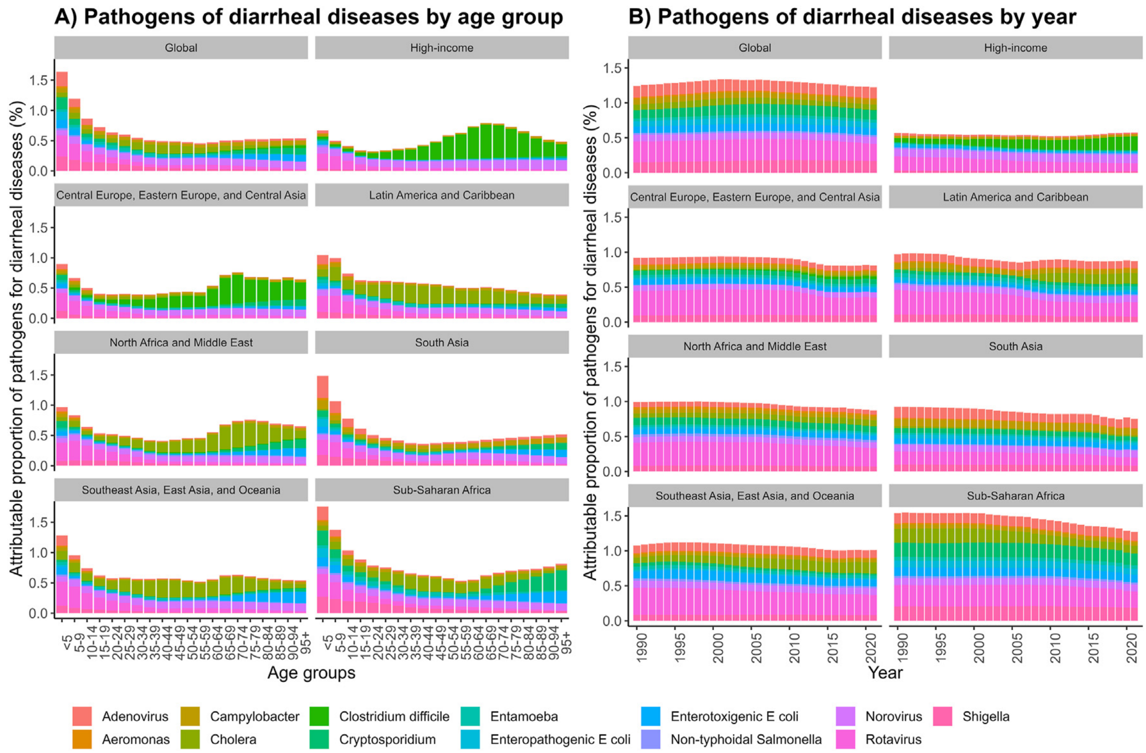

Fig. 4. Changes in the proportion of age-standardized DALY rates attributed to 13 pathogens of diarrheal diseases in different regions, 1990−2021. A: Changes by age group. B: Changes by year. Abbreviation: DALY, disability adjusted life year.

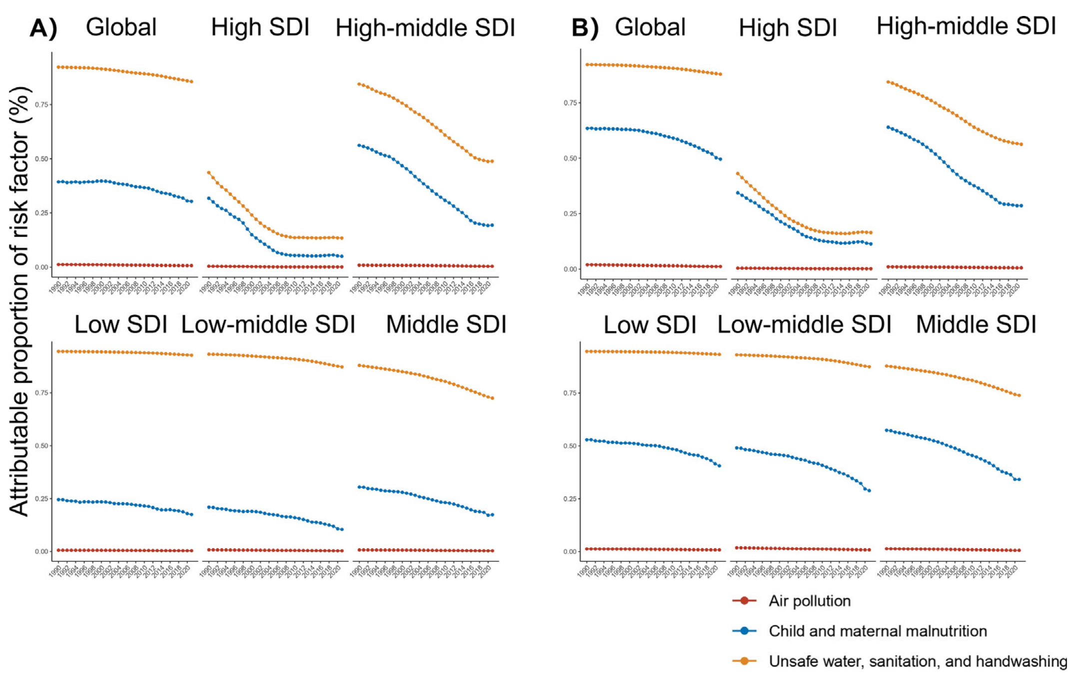

Fig. 5. The proportion of age-standardized rates for diarrheal diseases attributed to risk factors across regions of different SDI levels, 1990−2021. A: Age-standardized mortality rate. B: Age-standardized DALY rate. Abbreviations: DALY, disability adjusted life year; SDI: Socio-demographic index.

as census, insurance data, disease registries, death registry data, surveys, population studies, and scientific literature [44]. Adding the necessity for internal consistency, such as ensuring that cause-specific mortality aligns with all-cause mortality, will further increase the complexity. Moreover, the GBD employs comprehensive measures, such as DALYs and healthy life expectancy. These indicators may not reflect the scale of population receiving timely intervention or treatments [45]. Further efforts with diverse tracing indicators of health outcomes should be considered to comprehensively assess the disease burden and progress for the prevention and control of enteric infections.

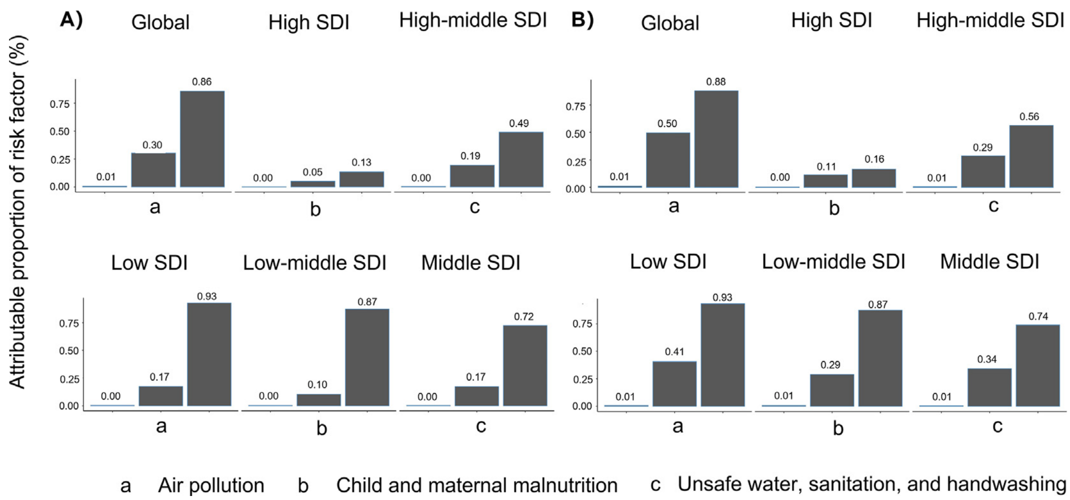

Fig. 6. The proportion of age-standardized rates for diarrheal diseases attributed to risk factors across regions of different SDI levels, 2021. A: Age-standardized mortality rate. B: Age-standardized DALY rate. Abbreviations: DALY, disability adjusted life year; SDI, Socio-demographic index.

5. Conclusion

This study, based on GBD 2021, evaluated the up-to-date global, regional, and national patterns of enteric infections in ASIR, ASMR, and age-standardized DALY rate over 204 countries and territories. The results underscored the importance of socio-economic development, health literacy, pathogen controls, and environmental improvements through a One Health approach. Targeted interventions in high-burden regions and populations, particularly in Sub-Saharan Africa and among children under five, might make significant strides toward improving global health and reducing the impact of enteric infections.

Ethics approval and consent to participate

Not applicable.

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Availability of data and materials

Data are available from GBD 2021. Public-use data can be retrieved from https://vizhub.healthdata.org/gbd-results/.

Consent for publication

Not applicable.

CRediT authorship contribution statement

Tianyun Li: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Conceptualization. **Ne Qiang:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Yujia Bao:** Writing – review & editing, Visualization, Validation. **Yongxuan Li:** Writing – review & editing, Visualization, Validation. **Shi Zhao:** Writing – review & editing. **Ka Chun Chong:** Writing – review & editing. **Xiaobei Deng:** Writing – review & editing. **Xiaoxi Zhang:** Writing – review & editing, Validation. **Jinjun Ran:** Writing – review & editing, Visualization, Validation, Formal analysis, Data curation. **Lefei Han:** Writing – review & editing, Visualization, Validation, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.soh.2024.100075.

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