

# Global, regional and national burden of dietary iron deficiency from 1990 to 2021: a Global Burden of Disease study

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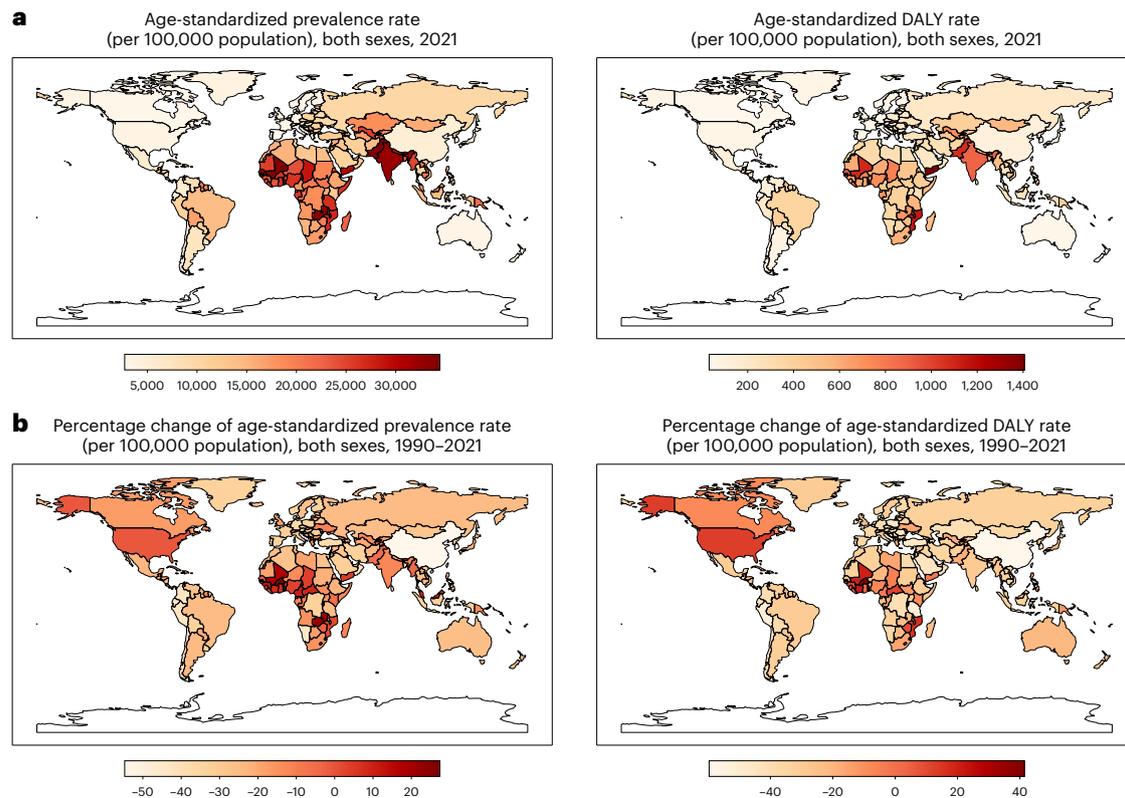
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Although iron deficiency is well documented, less is known about dietary involvement in symptomatic iron deficiency manifesting in medical conditions. In this study, we quantified the global burden of dietary iron deficiency, focusing on where inadequate dietary iron intake leads to clinical manifestations such as anemia. We analyzed data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 to estimate dietary iron deficiency prevalence and disability-adjusted life years (DALYs), stratified by age, sex, geography and socio-demographic index (SDI) across 204 countries. In 2021, global age-standardized prevalence and DALY rates were 16,434.4 (95% uncertainty interval (UI), 16,186.2–16,689.0) and 423.7 (285.3–610.8) per 100,000 population, with rates decreasing by 9.8% (8.1–11.3) and 18.2% (15.4–21.1) from 1990 to 2021. A higher burden was observed in female individual (age-standardized prevalence, 21,334.8 (95% UI, 20,984.8–21,697.4); DALYs, 598.0 (402.6–854.4)) than in male individual ((age-standardized prevalence, 11,684.7 (11,374.6–12,008.8); DALYs, 253.0 (167.3–371.0)). High-SDI countries presented greater improvement, with a 25.7% reduction compared to 11.5% in low-SDI countries. Despite global improvements, dietary iron deficiency remains a major health concern with a global prevalence of 16.7%, particularly affecting female individuals, children and residents in low-SDI countries. Urgent interventions through supplementation, food security measures and fortification initiatives are essential.

Iron deficiency is one of the most common micronutrient deficiencies, leading to iron deficiency anemia and causing a substantial disease burden worldwide<sup>1</sup>. Although it is considered relatively preventable with iron supplementation<sup>1</sup>, dietary iron deficiency is ranked as the eighth highest modifiable cause of years lived with disability (YLDs) in 2021 across all age groups, underscoring its global importance<sup>2</sup>. Previous studies highlighted infants, young children and pregnant people as particularly susceptible to dietary iron deficiency due to their high demand for supplementary iron<sup>3</sup>. Iron deficiency in

infants and children can impair brain development, metabolism and immune system development, and maternal iron deficiency is associated with an increased risk of preterm birth, low birth weight and adverse neonatal outcomes, leading to substantial associated disease burden and health consequences<sup>4,5</sup>.

Earlier research focused primarily on investigating the global burden of anemia<sup>4</sup>, with limited data on dietary iron deficiency at a global scale. Although one study estimated the global burden of micronutrient deficiency, it only provided prevalence rates of dietary



**Fig. 1 | Global map of age-standardized prevalence and DALY rates of dietary iron deficiency and their percentage changes over time, both sexes combined, 2021. a,b.** Age-standardized prevalence and DALY rates for dietary iron deficiency (a) and percentage changes of age-standardized prevalence and DALY rates for dietary iron deficiency (b).

iron deficiency at the country level, with limited subgroup analysis for each sex and age group<sup>6</sup>. Given the known disparities in dietary iron deficiency across demographics, subgroup analysis is crucial to prioritize high-risk populations requiring urgent resource allocation and tailored strategies for effective prevention and management<sup>1</sup>. Moreover, previous studies on dietary iron deficiency often assessed disease burden based solely on iron levels, which may capture cases of iron deficiency without clinical symptoms or those of lesser clinical relevance, potentially overestimating the overall burden<sup>7,8</sup>.

This Global Burden of Disease (GBD) Study 2021 analysis focused on complicated dietary iron deficiency—specifically individuals presenting with anemia—to better capture the impact of such cases and identify high-priority populations for dietary interventions. We estimated the prevalence and burden (that is, DALYs) associated with dietary iron deficiency across 204 countries and territories from 1990 to 2021.

## Results

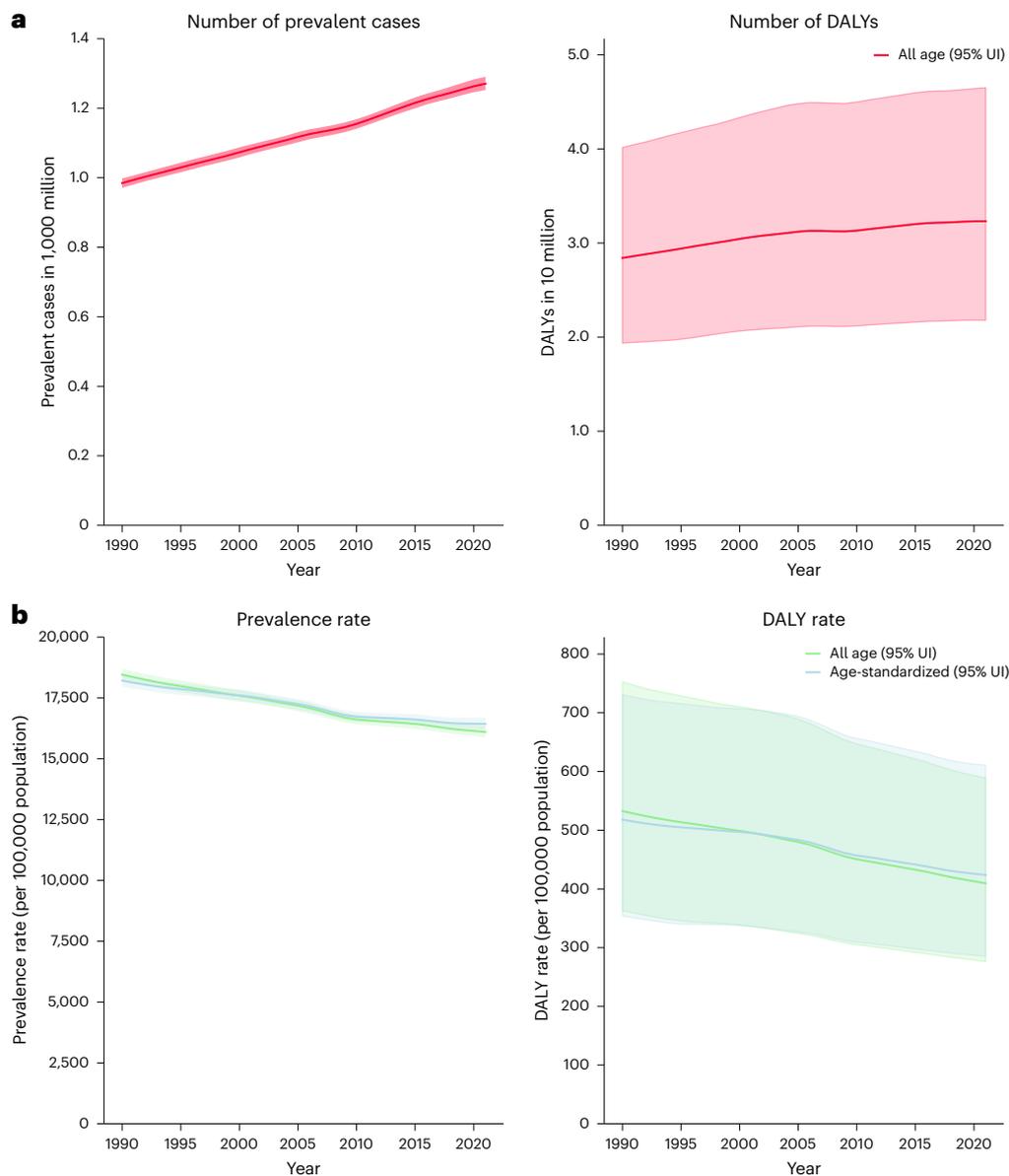
### Global burden of dietary iron deficiency

In 2021, the global age-standardized prevalence and DALY rates of dietary iron deficiency were 16,434.4 (95% UI, 16,186.2–16,689.0) and 423.7 (285.3–610.8) per 100,000 population, respectively (Supplementary Table 6). The all-age global prevalence of dietary iron deficiency was 16.7% (95% UI, 16.4–16.9). These country-level age-standardized rates and their percentage changes are presented in Fig. 1. The number of prevalent cases worldwide increased by 29.0%, from 984.6 (95% UI, 970.8–997.8) million in 1990 to 1,270.6 (1,252.4–1,290.7) million in 2021, as illustrated in Fig. 2. Detailed numbers of cases and age-standardized rates of prevalence and DALYs for each SDI region are presented in Supplementary Tables 7–11. In Tables 1 and 2, the percentage changes of age-standardized rates of prevalence and

DALYs for each decade are presented. The global age-standardized prevalence rate and DALY rate decreased by 9.8% (95% UI, 8.1–11.3) and 18.2% (15.4–21.1) from 1990 to 2021, respectively. From 2000 to 2010, the prevalence rate decreased by 5.0% (95% UI, 4.1–5.9), the most considerable reduction observed, whereas the lowest change was observed between 2019 and 2021, with a decline of 0.1% (–0.6 to 0.4). Similarly, the DALY rate was the most substantially reduced between 2000 and 2010 (8.1% (95% UI, 6.5–9.9)) and between 2010 and 2019 (8.6% (6.3–11.4)), with the smallest reduction between 2019 and 2021, at 1.0% (0.3–1.8).

### Burden of dietary iron deficiency according to age and sex

Global ranks and distributions of dietary iron deficiency according to each age group are depicted in Extended Data Figs. 1–7. Dietary iron deficiency ranked particularly high among those aged 5–14 years in low and lower-middle SDI countries. Subgroup analysis presented in Fig. 3 revealed that female individuals had higher prevalence rates than male individuals in age groups under 65 years. DALY rates were higher in female than in male individuals across all ages, particularly during reproductive years. In 2021, the age-standardized prevalence rates per 100,000 population were 21,334.8 (20,984.8–21,697.3) in female and 11,684.7 (11,374.6–12,008.8) in male individuals. Similarly, the age-standardized DALY rates per 100,000 population were higher in female individuals (598.0 (402.6–854.4)) than in male individuals (253.0 (167.2–370.9)) (Supplementary Tables 12 and 13). However, from 1990 to 2021, a greater decrease was observed among male individuals (20.6% (18.3–23.0)) compared to female individuals (2.6% (0.6–4.5)). Considerable differences were observed among age groups, with children aged 6–11 months and adults over 95 years showing substantial burdens compared to other age groups (Supplementary Table 14). Similar patterns were observed for each sex (Supplementary Tables 15 and 16).



**Fig. 2 | Numbers and rates of dietary iron deficiency, 1990–2021. a, b.** Number of prevalent cases and DALYs of dietary iron deficiency at the global level (**a**) and rates (per 100,000 population) of age-standardized and all-age prevalence and DALYs of dietary iron deficiency at the global level (**b**). The lines represent the

central estimate (median) of the number and rate. Uncertainty was incorporated at every stage of the estimation process by random sampling from possible value ranges for each estimate. The final UI for each result was determined using the 2.5th and 97.5th percentiles of the draws.

### Burden of dietary iron deficiency by SDI and region

There were substantial disparities in age-standardized dietary iron deficiency prevalence rates among SDI quintiles (Supplementary Tables 7–11). In 2021, lower SDI countries exhibited higher age-standardized prevalence rates per 100,000 population compared to higher SDI countries (low SDI, 27,301.1 (26,624.0–27,996.5); lower-middle SDI, 25,686.6 (25,141.4–26,256.7); middle SDI, 13,569.0 (13,297.7–13,840.1); higher-middle SDI, 8,010.2 (7,718.0–8,300.7); high SDI, 4,572.6 (4,338.6–4,812.6)). A similar pattern was observed in DALY rates (low SDI, 756.7 (507.9–1,079.0); lower-middle SDI, 701.7 (473.8–995.6); middle SDI, 325.7 (217.3–471.7); higher-middle SDI, 158.5 (105.2–230.7); high SDI, 71.1 (46.7–107.1)).

Figure 4 presents the male-to-female (M/F) ratio of dietary iron deficiency, comparing both prevalence and DALY rates across age groups and SDI levels. Female participants exhibited a markedly higher prevalence of dietary iron deficiency during childhood and

reproductive ages compared to male participants, with this disparity being most pronounced in high-SDI countries. Specifically, in high-SDI countries, the M/F prevalence ratio was 0.1 among the age group between 25 years and 29 years, whereas low-SDI countries exhibited a ratio of 0.3 for the same age group. This pattern shifted in older populations, where high-SDI countries showed a higher burden in male adults compared to female adults (M/F ratio of 1.7 for ages 80–84 years), whereas low-SDI countries (ratio of 1.1 for the same age group) maintained a relatively similar burden distribution between sexes. Similar patterns were also observed for DALY rates (Supplementary Tables 17 and 18).

Disparities in both age-standardized prevalence and DALY rates were observed across world regions (Supplementary Tables 19–21). The highest prevalence and DALY rates were observed in South Asia (prevalence per 100,000 population, 31,696.8 (95% UI, 31,046.8–32,415.5); DALYs, 885.5 (95% UI, 600.3–1,271.4)) and Western Sub-Saharan Africa

**Table 1 | Prevalence of dietary iron deficiency, 1990–2021**

	Percentage change in prevalence (95% UI)				
	1990–2021	1990–2000	2000–2010	2010–2019	2019–2021
Global (overall)					
Absolute number	29,050 (26,883 to 31,362)	8,998 (7,872 to 10,247)	7,624 (6,519 to 8,623)	11,934 (10,085 to 13,673)	1,350 (0,897 to 1,802)
Age-standardized rate	-9.762 (-11.256 to -8.109)	-3.318 (-4.287 to -2.287)	-4.982 (-5.919 to -4.116)	-2.145 (-3.832 to -0.468)	-0.092 (-0.550 to 0.376)
Sex					
Male					
Absolute number	12,081 (8,835 to 15,494)	5,993 (4,146 to 7,809)	2,040 (0,309 to 3,780)	4,433 (1,100 to 7,523)	0,013 (-0,894 to 0,903)
Age-standardized rate	-20.605 (-22,951 to -18,246)	-5.263 (-6,798 to -3,709)	-9.500 (-10,978 to -7,957)	-8.786 (-11,733 to -6,056)	-1.151 (-2,047 to -0,279)
Female					
Absolute number	40,503 (37,698 to 43,346)	11,026 (9,627 to 12,482)	11,222 (9,958 to 12,384)	16,381 (14,399 to 18,406)	2,084 (1,665 to 2,548)
Age-standardized rate	-2.577 (-4.503 to -0.610)	-2.153 (-3.312 to -0.947)	-2.128 (-3.203 to -1.120)	1.999 (0.167 to 3.878)	0.530 (0.110 to 1.006)
SDI					
Low SDI					
Absolute number	95,343 (88,846 to 102,106)	25,432 (22,873 to 28,172)	22,035 (19,202 to 24,961)	32,844 (28,398 to 37,279)	4,094 (2,923 to 5,190)
Age-standardized rate	-11.523 (-13,987 to -8,836)	-3.694 (-5,348 to -1,933)	-6.253 (-7,999 to -4,367)	-2.338 (-5,231 to 0,554)	-0.485 (-1,420 to 0,403)
Lower-middle SDI					
Absolute number	38,782 (34,797 to 43,389)	14,585 (12,495 to 16,932)	10,510 (8,602 to 12,494)	11,501 (8,297 to 14,431)	1,035 (0,307 to 1,803)
Age-standardized rate	-14.993 (-17,178 to -12,483)	-4.016 (-5,567 to -2,340)	-6.008 (-7,444 to -4,446)	-6.814 (-9,250 to -4,519)	-1.105 (-1,771 to -0,385)
Middle SDI					
Absolute number	9,748 (7,324 to 12,229)	3,357 (1,797 to 4,896)	2,265 (0,857 to 3,636)	4,615 (2,600 to 6,848)	0,302 (-0,273 to 0,864)
Age-standardized rate	-22.017 (-23,733 to -20,340)	-7.522 (-8,906 to -6,237)	-9.366 (-10,608 to -8,129)	-8.294 (-10,124 to -6,215)	-0.951 (-1,558 to -0,384)
Higher-middle SDI					
Absolute number	-19,825 (-22,632 to -16,572)	-3,535 (-5,599 to -1,286)	-10,763 (-12,739 to -8,711)	-8,089 (-11,053 to -4,583)	-1,341 (-2,265 to -0,414)
Age-standardized rate	-34.429 (-36,910 to -31,689)	-9.773 (-11,781 to -7,620)	-17.901 (-19,999 to -15,816)	-13.763 (-16,757 to -9,972)	-1.215 (-2,223 to -0,193)
High SDI					
Absolute number	-3,863 (-10,933 to 3,880)	-14,041 (-18,852 to -9,637)	6,276 (2,254 to 11,008)	6,246 (-0,102 to 12,844)	0,693 (-0,848 to 2,284)
Age-standardized rate	-25.749 (-31,078 to -19,700)	-20.191 (-24,397 to -16,301)	-3.845 (-7,750 to 0,316)	-3.845 (-9,819 to 2,948)	-0.538 (-2,293 to 1,231)

(prevalence, 26,171.5 (95% UI, 25,195.0–27,200.2); DALYs, 708.8 (95% UI, 461.7–1,016.5)), respectively. The greatest reduction in prevalence rate was observed in East Asia with a decline of 53.9% (52.7–55.1). Western Sub-Saharan Africa was the only region with a possible increasing trend in prevalence rate (4.9% (95% UI, -1.4 to 10.9)) compared to other regions. The percentage change for each region is presented in Supplementary Tables 22 and 23.

## Discussion

We investigated the global, regional and national burden of dietary iron deficiency using estimates from GBD 2021. The total number of people with dietary iron deficiency increased from 1990 to 2021, likely due to population growth, as age-standardized prevalence rates

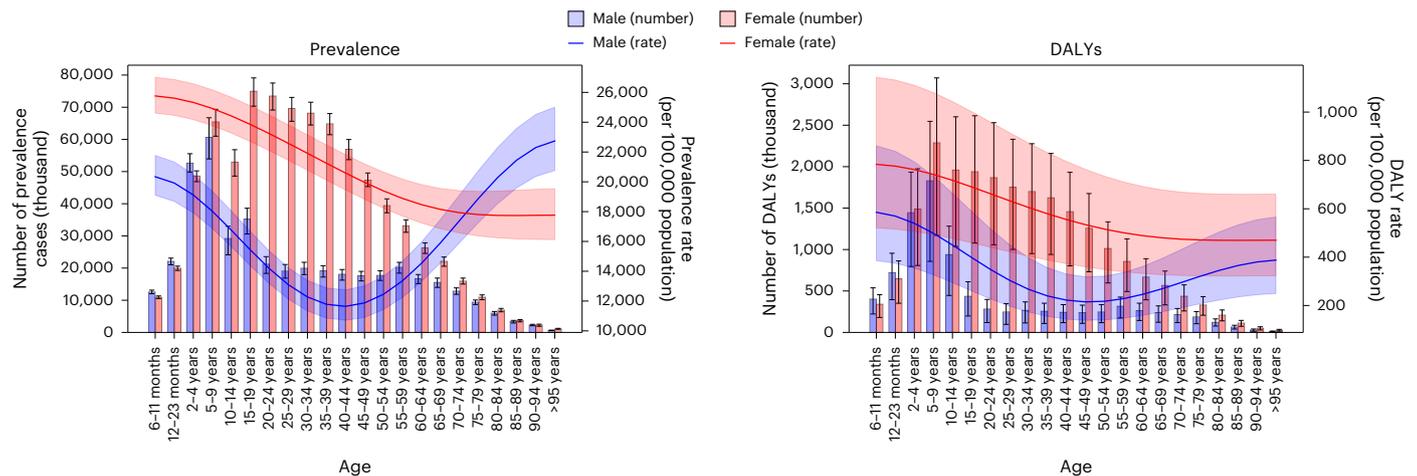
decreased during the same period. A decrease in age-standardized DALY rates for dietary iron deficiency over time might suggest improvements in nutritional deficiency management. Female participants generally showed higher prevalence and DALY rates than male participants, with the reduction in prevalence rates for female participants over time being much smaller than male participants. Those aged 6–11 months particularly had a higher burden compared to other age groups for both sexes. Moreover, individuals from low-SDI countries exhibited a higher burden of dietary iron deficiency. These findings underscore the urgent need for targeted interventions to address the persistent burden of dietary iron deficiency, particularly among female individuals, young children and populations in low-SDI countries.

**Table 2 | DALYs associated with dietary iron deficiency, 1990–2021**

	Percentage change in DALYs (95% UI)				
	1990–2021	1990–2000	2000–2010	2010–2019	2019–2021
Global (overall)					
Absolute number	13,763 (9,907 to 17,608)	7,133 (5,321 to 9,034)	2,900 (0,937 to 4,720)	3,870 (1,001 to 6,432)	0,164 (–0,571 to 0,846)
Age-standardized rate	–18,194 (–21,089 to –15,413)	–4,029 (–5,563 to –2,404)	–8,096 (–9,862 to –6,479)	–8,630 (–11,357 to –6,269)	–1,040 (–1,817 to –0,333)
Sex					
Male					
Absolute number	–9,687 (–15,248 to –3,261)	1,925 (–1,041 to 5,096)	–6,084 (–9,877 to –2,632)	–6,539 (–12,581 to –1,029)	–1,668 (–3,361 to –0,227)
Age-standardized rate	–32,001 (–36,127 to –27,471)	–6,777 (–9,364 to –4,220)	–14,949 (–18,313 to –11,962)	–16,918 (–22,450 to –11,985)	–2,177 (–3,841 to –0,767)
Female					
Absolute number	27,285 (23,164 to 31,640)	10,136 (7,979 to 12,149)	7,695 (5,803 to 9,531)	8,732 (5,906 to 11,627)	0,933 (0,171 to 1,663)
Age-standardized rate	–10,518 (–13,610 to –7,454)	–2,589 (–4,464 to –0,791)	–4,489 (–6,189 to –2,777)	–4,555 (–7,224 to –1,860)	–0,530 (–1,276 to 0,209)
SDI					
Low SDI					
Absolute number	69,446 (58,228 to 80,568)	19,918 (15,034 to 24,525)	17,063 (11,752 to 22,024)	24,677 (18,051 to 31,333)	2,837 (1,346 to 4,303)
Age-standardized rate	–21,962 (–26,053 to –17,656)	–8,327 (–11,468 to –5,575)	–9,355 (–12,566 to –6,082)	–7,133 (–11,464 to –2,749)	–1,383 (–2,671 to –0,216)
Lower-middle SDI					
Absolute number	14,567 (8,001 to 20,954)	10,118 (7,005 to 13,632)	3,768 (0,599 to 6,968)	0,491 (–4,116 to 5,024)	–0,764 (–2,030 to 0,524)
Age-standardized rate	–28,029 (–31,919 to –24,335)	–7,182 (–9,671 to –4,545)	–10,927 (–13,365 to –8,510)	–15,236 (–18,955 to –11,721)	–2,648 (–3,778 to –1,478)
Middle SDI					
Absolute number	–4,461 (–8,018 to –0,694)	1,364 (–0,714 to 3,293)	–2,006 (–3,977 to 0,010)	–4,475 (–7,550 to –1,539)	–0,861 (–1,633 to –0,103)
Age-standardized rate	–29,420 (–32,204 to –26,600)	–8,211 (–10,038 to –6,663)	–11,654 (–13,541 to –9,922)	–15,439 (–18,267 to –12,761)	–1,821 (–2,610 to –1,055)
Higher-middle SDI					
Absolute number	–31,821 (–35,802 to –27,884)	–5,916 (–8,925 to –3,070)	–18,533 (–21,383 to –15,896)	–13,183 (–16,734 to –9,320)	–1,446 (–2,482 to –0,355)
Age-standardized rate	–43,702 (–46,865 to –40,316)	–11,520 (–14,315 to –8,814)	–24,340 (–26,931 to –22,036)	–19,129 (–22,902 to –15,491)	–1,387 (–2,492 to –0,112)
High SDI					
Absolute number	–6,470 (–12,819 to 0,244)	–12,024 (–15,597 to –8,706)	3,456 (–0,784 to 7,464)	3,102 (–3,619 to 9,555)	1,231 (–0,146 to 2,639)
Age-standardized rate	–27,549 (–32,203 to –22,470)	–18,422 (–21,708 to –15,359)	–6,168 (–10,028 to –2,414)	–6,531 (–12,225 to –0,610)	–0,038 (–1,522 to 1,280)

Previous studies predominantly focused on all-cause anemia or all-cause iron deficiency, with limited studies specifically addressing dietary iron deficiency. From a public health perspective, understanding dietary iron deficiency is crucial as it represents a preventable burden that can be addressed through feasible interventions. A recent pooled iron level analysis revealed that iron deficiency rates among preschool-aged children were higher than 20% in 13 countries and 10–19% in 8 other countries<sup>7</sup>. Similarly, for non-pregnant reproductive-age people, 10 datasets indicated prevalence rates exceeding 20%, with six datasets showing between 10% and 19%<sup>7</sup>. However, this analysis was limited by its exclusion of men, school-aged children and older adults and coverage of only 22 countries with median data collection in 2013. Another study by Passarelli et al.<sup>8</sup> estimated the

global prevalence of dietary iron deficiency to be 65%—substantially higher than the 16.7% found in our analysis. This large variation likely reflects differences in scope and case definitions; Passarelli et al.<sup>8</sup> accounted for both complicated and uncomplicated iron deficiency cases by analyzing iron level data, whereas this GBD centered on dietary iron deficiency related to anemia, representing symptomatic or complicated cases. We aimed to estimate the global burden of complicated dietary iron deficiency to better capture its impact and identify high-priority populations for dietary interventions. Despite these differences, both our analysis and that of Passarelli et al.<sup>8</sup> consistently showed higher prevalence among female individuals and in lower SDI regions, particularly in South Asian and sub-Saharan African countries. The convergence of findings across different methodologies



**Fig. 3 | Numbers and age-specific rates (per 100,000 population) of prevalence and DALYs from dietary iron deficiency at the global level by age group and sex, 2021.** The bars and lines represent the central estimate (median) of the number and rate, respectively. The error bars represent uncertainty, which was

incorporated at every stage of the estimation process by random sampling from possible value ranges for each estimate. The final uncertainty interval for each result was determined using the 2.5th and 97.5th percentiles of the draws.

underscores the importance of urgent global action to reduce dietary iron deficiency, especially in at-risk populations.

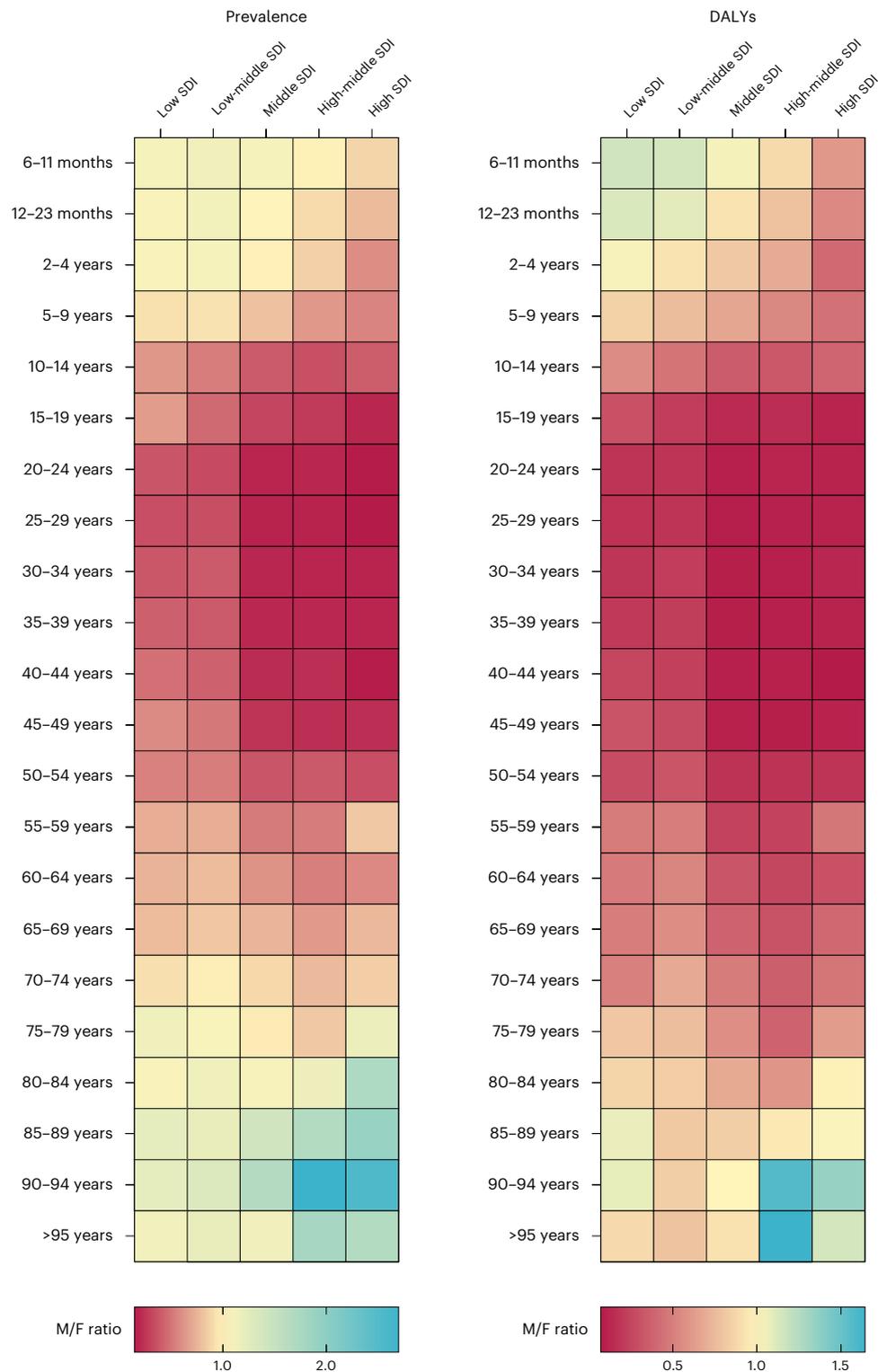
From 1990 to 2021, the age-standardized prevalence rate of dietary iron deficiency declined worldwide, a trend attributable to several factors. The inclusion of anemia in the United Nations' Sustainable Development Goals (SDGs) prompted substantial and widespread policy actions<sup>9</sup>. Nutrition programs, such as iron supplementation for pregnant people and children, as well as food fortification with iron-containing multiple micronutrient powders, were recommended by the World Health Organization (WHO)<sup>10</sup>. These policies likely contributed to the reduction in the prevalence of dietary iron deficiency, particularly in low- and middle-income countries (LMICs) with high rates of severe anemia<sup>11</sup>. Furthermore, studies indicated that countries experiencing economic growth have seen increased access to animal-source foods and implementation of iron fortification programs, resulting in improvements in nutritional status<sup>12</sup>. The correlation between diversifying food supplies and lower rates of anemia, malnutrition and stunting was suggested<sup>12</sup>. This could account for the higher prevalence of anemia from dietary iron deficiency in lower SDI countries, where food supply and diversity are often limited<sup>13</sup>.

Substantial differences between sexes and age groups were also observed in our study. Female individuals had higher prevalence rates than male individuals in age groups under 65 years, and DALY rates were higher in female individuals across all ages, particularly during reproductive years. One possible reason for the sex differences in the prevalence of dietary iron deficiency is that female individuals, particularly those of reproductive age, face higher demands for iron due to menstrual blood loss and childbirth<sup>6</sup>; previous studies indicated that iron stores in pre-menopausal women are substantially influenced by menstrual blood loss, requiring more iron intake to sustain essential body function<sup>14</sup>. In addition to menstrual blood loss, sex-hormonal influences also play a critical role in iron metabolism. Estrogen, which rises during the reproductive years, is known to affect iron absorption and distribution, further emphasizing why women of reproductive age require higher dietary iron intake<sup>3</sup>. Similarly, pregnancy imposes an additional burden on iron stores as fetal development significantly increases iron demands<sup>14</sup>. Such life stages create fluctuations in body iron demand throughout a woman's life, potentially increasing vulnerability to even marginal changes in dietary iron intake. This is distinct from cases where pathological conditions, such as heavy menstrual bleeding or other menstrual disorders, are the primary cause of iron deficiency, which are categorized separately in our analysis. In addition to the increased

physiological iron requirements of female individuals of reproductive age, a range of complex and interrelated factors may contribute. Studies suggest that variations in dietary access and food choices, influenced by socioeconomic contexts—such as unequal food distribution within households and limited dietary diversity—disproportionately affect female individuals, particularly those from low-income households<sup>15</sup>.

Conversely, post-menopausal women typically experience a decrease in iron loss due to the cessation of menstruation, which can lead to relatively higher iron stores<sup>1</sup>. However, older adults, regardless of sex, may still face iron deficiency due to factors such as reduced dietary intake, chronic diseases or decreased gastrointestinal absorption. Therefore, although reproductive-age women are particularly vulnerable, age-related physiological changes also substantially impact iron status across the lifespan. In older age groups, we observed no significant sex differences in dietary iron deficiency, with a slightly higher prevalence rate in male adults. This pattern may be explained by age-related testosterone decline in male adults, which reduces hemoglobin and hematocrit levels and may increase iron demands<sup>16</sup>.

SDG 2, which primarily focuses on achieving zero hunger, also includes efforts to improve nutrition and address malnutrition, such as reducing the prevalence of anemia among women of reproductive age by 2030. This aligns with its broader objectives to enhance health outcomes for vulnerable populations<sup>9</sup>. However, our data suggest that progress toward this goal has been minimal, particularly in LMICs. The recent impacts of the COVID-19 pandemic have further exacerbated existing challenges. We think that this limited advancement can be attributed to several complex and interrelated factors. Global food supply chain disruptions, intensified by the pandemic, have impacted the availability and affordability of nutrient-rich foods in low-SDI countries. This impact has been particularly severe in LMICs, where existing food distribution infrastructure is often unstable<sup>17</sup>. Compared to high-income countries, healthy diets with sufficient nutrients are more difficult to afford in LMICs<sup>18</sup>. Furthermore, economic crises at national and household levels have led to increased food insecurity, making it challenging for people to afford a nutrient-adequate diet<sup>19</sup>. Fruits, vegetables and animal-source foods, which are rich in essential nutrients, including iron, remain comparatively costly sources of calories in contrast to starchy staples and cereals in LMICs<sup>20</sup>. These cost disparities often force families to rely heavily on less nutritious but more affordable food options, a scenario exacerbated during the pandemic<sup>17</sup>, which altogether may partly explain the minimal reduction in global dietary iron deficiency burden observed during this period



**Fig. 4 | The M/F ratio of prevalence and DALY rates (per 100,000 population) of dietary iron deficiency by SDI and age group, 2021.** M/F ratio of dietary iron deficiency burden in 2021 is shown across age groups and SDI quintiles. The left panel represents the M/F ratio of age-specific prevalence rates (per 100,000 population), and the right panel displays the M/F ratio of DALYs per 100,000

population. Rows indicate age groups, ranging from 6–11 months to more than 95 years, and columns correspond to SDI quintiles, from low to high. In both panels, color gradients reflect the M/F ratio, with darker red shades indicating higher M/F ratios and blue-green shades representing lower ratios.

(Tables 1 and 2). The situation is further complicated by armed conflicts in various regions, which have intensified food insecurity, trade routes, agriculture and disrupted health systems<sup>21</sup>. Climate change also influences food availability and nutritional quality as it impacts crop yields and food production patterns<sup>22</sup>.

Despite global efforts to reduce dietary iron deficiency, its prevalence has only slightly decreased, falling short of the SDG targets. This persistent challenge highlights ongoing disparities in global food security and resource allocation, reflecting the complex interplay of economic, environmental and political factors influencing nutrition

worldwide. Given the particular susceptibility of populations in LMICs to malnutrition and related health burdens, it is crucial to bolster global efforts to stabilize global food supply chains and enact targeted policies.

Recognizing the relationship between dietary iron deficiency and nutritious diet access highlights the need for social services to support those lacking such diets. Ensuring continued delivery of nourishing school meals through home delivery, take-home rations and vouchers when schools are closed might be crucial in some regions<sup>23</sup>. Universal free school meals are one of the options to support nutrition and academic equity for all children and adolescents<sup>24</sup>. Additionally, income support for low-income households can reduce food insecurity, underscoring the importance of social protection<sup>25</sup>. The provision of iron supplements to at-risk populations could be considered a straightforward public health approach. This can be accomplished through various strategies, including supplementation, fortification of staple foods and the use of multiple micronutrient powders<sup>26</sup>. Targeted promotions aimed at populations with inadequate iron intake can effectively alleviate the burden of iron deficiency. A previous study reported that prenatal iron supplementation can reduce maternal anemia by 70%<sup>27</sup>, suggesting the potential for implementation. However, challenges remain due to limited access to prenatal care or iron supplementation, particularly among individuals at low socioeconomic status<sup>28</sup>.

With 2030 approaching, it is clear that considerable efforts are still required to meet the broader SDG 2 target, within which reducing anemia is one of the sub-goals. The WHO has set a target to achieve a 50% reduction in the prevalence of anemia among women of reproductive age (15–49 years) by 2025, as part of its Global Nutrition Targets 2025 (ref. 9). Our analysis of the population-level burden of dietary iron deficiency can provide the insights required to appropriately tailor interventions at the national and regional levels in an effort to reduce the prevalence across all age and sex groups. Our estimates can have implications for determining funding allocations, shaping programmatic priorities and supporting advocacy initiatives, all of which are imperative to achieving the targets set by the SDGs.

This study has several limitations. It relies on estimates derived from GBD methodology, where there are potential biases that need to be considered. Because complete data on dietary iron deficiency were not available for all 204 countries, missing data were supplemented through the GBD modeling process. Consequently, the actual level of dietary iron deficiency in certain regions or countries may have been either overestimated or underestimated, and results may be presented with broad and overlapping uncertainty intervals. Therefore, when interpreting the estimates, it is crucial to carefully consider each country's or region's data collection environment and the potential for missing information, acknowledging that the true prevalence of dietary iron deficiency may be higher or lower than the reported estimates<sup>2</sup>. Our methodology did not capture non-anemic iron deficiency with normal hemoglobin concentration, which could potentially lead to an underestimation of the total disease burden. However, current evidence indicates that the most substantial adverse health outcomes of iron deficiency manifest when hemoglobin levels decrease to the point of anemia<sup>4,26,29</sup>, justifying our focus on symptomatic/complicated dietary iron deficiency. Moreover, when compared to other GBD disability weights, mild anemia has one of the lowest disability weights across all categories: mild anemia (0.004), moderate anemia (0.052) and severe anemia (0.149). This suggests that non-anemic iron deficiency, with presumably even lower disability weights, could minimally contribute to burden estimates. However, it would also substantially increase case counts, which could overestimate iron deficiency prevalence due to the potential inclusion of individuals without anemia. By limiting to anemic iron deficiency attributable to inadequate diet, our approach estimated clinically significant burden associated with a dietary component. Third, the current modeling framework falls short in fully distinguishing dietary deficiencies from

other causes due to the lack of richer and more integrated data sources that provide direct, simultaneous measurement of dietary intake and menstrual health factors as well as other contributing conditions for iron deficiency. Finally, this study did not account for the role of ethnicity in the burden of dietary iron deficiency. Previous research indicates significant variations in hemoglobin concentrations among different ethnic groups, with East Asians exhibiting higher concentrations than African Americans<sup>30</sup>.

This study also has several strengths. It estimated the burden of iron deficiency due to inadequate nutrition, facilitating a direct estimation of the iron deficiency burden that can potentially be prevented by diet interventions. Given that dietary iron deficiency is the largest contributor to anemia (Extended Data Fig. 8) and can be modified through relatively simple dietary measures, our targeted focus allows us to identify population groups that could benefit from accessible interventions, such as iron supplements. In contrast to previous studies that broadly encompassed non-anemic iron deficiency, we focused on iron deficiency manifesting as anemia to better capture the clinical impact of iron deficiency and prioritize food resources. Lastly, the data highlighted demographics most susceptible to dietary iron deficiency by examining disease burden across age groups and sexes, with potential insights for policymakers looking to tailor public health actions to specific populations.

In conclusion, dietary iron deficiency remained a prevalent and persistent global burden, with a global prevalence of 16.7%, despite a decreasing trend globally from 1990 to 2021. Dietary iron deficiency disproportionately affected women, children and populations residing in the African continent and in low-SDI countries. Given that dietary iron deficiency can be effectively managed through interventions such as iron supplements, balanced diets and fortified foods, urgent and universal actions are warranted. Further research should focus on integrating data from diverse sources, including food systems, dietary intake patterns and population health metrics, to gain a more comprehensive understanding of dietary iron deficiency.

## Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41591-025-03624-8>.

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## Methods

### Overview

This paper was produced as part of the GBD Collaborator Network and in accordance with the GBD Protocol<sup>9</sup>. The GBD 2021 offers a comprehensive evaluation of the global disease burden, quantifying health loss from 371 diseases across 204 countries and territories between 1990 and 2021 (ref. 2). This work involved collaboration from over 10,000 experts in more than 150 countries, contributing to data provision, analysis and review necessary for generating GBD metrics, such as incidence, prevalence, cause-specific mortality, years of life lost, YLDs and DALYs. The present study specifically targeted dietary iron deficiency, distinguishing it from other forms of iron deficiency. We aimed to assess the health burden arising directly from undernutrition, thereby underscoring the importance of public health interventions focused on dietary improvement. This study adheres to the Guidelines for Accurate and Transparent Health Estimate Reporting (GATHER)<sup>2</sup> (Supplementary Table 1), with analyses conducted using R software version 4.3.2 (R Foundation) and Python version 3.11.4 (Python Software Foundation). The supplementary methods contain further details on specific methodologies.

### Case definition

Dietary iron deficiency is defined as iron deficiency directly resulting from inadequate dietary iron intake that is insufficient to meet the body's requirements<sup>2</sup>. This definition emphasizes iron deficiency as a modifiable public health burden and distinguishes it from other conditions caused by non-dietary factors such as chronic diseases, physiological conditions or metabolic disorders. This study models dietary iron deficiency as a preventable cause of anemia by focusing on cases where insufficient dietary iron intake leads to physiological complications<sup>31</sup>.

Menstruation increases physiological iron requirements, and when dietary intake does not meet these elevated needs, this is classified as dietary iron deficiency. However, pathological conditions, such as uterine fibroids or heavy menstrual bleeding, are modeled separately and are excluded from dietary iron deficiency estimates. This distinction ensures that dietary iron deficiency represents preventable cases solely attributable to insufficient dietary iron intake, independent of other pathological conditions. This study offers targeted nutritional strategies to mitigate dietary iron deficiency at the population level, providing a strong foundation for actionable public health policy. The scope of dietary iron deficiency excludes iron deficiency that occurs independent of dietary intake, and such non-dietary causes are modeled independently within the GBD framework<sup>2</sup> (Extended Data Fig. 9). Excluded causes include the following:

1. Neglected tropical diseases. Tropical diseases such as malaria, hookworm infections and schistosomiasis cause anemia through chronic blood loss or hemolysis, which is not related to dietary iron intake. These diseases are primarily addressed through disease management programs rather than nutritional interventions.
2. Gastrointestinal disorders. Gastrointestinal disorders, such as inflammatory bowel disease, chronic gastritis and ulcers, impair iron absorption or result in chronic blood loss. These conditions require clinical interventions beyond dietary therapy.
3. Chronic health conditions and metabolic disorders. Systemic diseases such as cirrhosis and chronic kidney disease affect iron metabolism or cause blood loss, which leads to anemia independent of dietary intake. These conditions require specialized medical management.
4. Reproductive health factors. Conditions such as heavy menstrual bleeding, uterine fibroids and maternal hemorrhage cause anemia through acute or chronic blood loss. Menstruation increases physiological iron requirements, but anemia that results from an inability to meet the increased need is classified as dietary iron deficiency. On the other hand, anemia caused

by a pathological condition (for example, uterine fibroids) is modeled separately.

5. Micronutrient deficiencies. Deficiencies of other micronutrients, such as vitamin A, can affect hemoglobin synthesis and iron metabolism, increasing the prevalence of anemia. To address this, a comprehensive nutritional strategy is needed, not just iron supplementation.

By restricting the study's focus to dietary iron deficiency, this analysis enables a more precise estimation that is directly preventable and manageable through dietary interventions. This approach emphasizes the need for targeted nutritional strategies to reduce dietary iron deficiency at the population level, aligning with public health policies aimed at alleviating undernutrition.

### Geographic locations of the analysis

We developed estimates for 204 countries and territories, categorized into 21 regions and 7 broad super-regions. The super-regions include Central Europe, Eastern Europe and Central Asia; High-Income; Latin America and the Caribbean; North Africa and the Middle East; South Asia; Southeast Asia, East Asia and Oceania; and sub-Saharan Africa. In GBD 2021, we continue to conduct subnational analyses for countries included in earlier cycles, such as Brazil, China, Ethiopia, India, Indonesia, Iran, Italy, Japan, Kenya, Mexico, New Zealand, Nigeria, Norway, Pakistan, Russia, the Philippines, Poland, South Africa, Sweden, the UK and the USA. Analyses are carried out at the first administrative level within each country, except for New Zealand (by Māori ethnicity), Sweden (by Stockholm and non-Stockholm areas), the UK (by local government authorities) and the Philippines (by provinces).

At the most granular spatial resolution, we generated estimates for 983 unique locations. As with GBD 2019, GBD 2021 continues to use a classification of standard and non-standard locations. Standard GBD locations encompass all subnationals from countries with high-quality data and populations exceeding 200 million, along with all other countries. This classification includes subnationals for China, India, the USA and Brazil but it excludes Indonesia; data for China, India, the USA and Brazil are also available at the national level. All other countries with subnational estimates are defined as non-standard locations.

### Input data and data processing

For GBD 2021, dietary iron deficiency estimates were derived using a substantial portion of data collected from population-based surveys, peer-reviewed studies and governmental reports<sup>32</sup>. These data sources included the Demographic and Health Survey, the Multiple Indicator Cluster Survey series, national micronutrient surveys and other nutrition surveillance systems at national and subnational levels. To account for regional and demographic variability, the modeling framework incorporated region-specific covariates, such as the Healthcare Access and Quality Index (HAQI), malaria prevalence, and child undernutrition indicators. These adjustments helped dietary iron deficiency estimates align more closely with population-specific dietary intake patterns while minimizing the influence of non-dietary factors.

During the data extraction process, we focused on demographic variables (such as location, sex and age), survey design variables (such as sampling strategy and sampling weights) and population estimate variables (such as prevalence or proportion), along with measures of uncertainty (such as standard error, confidence interval, sample size and number of cases). Using available microdata, data were categorized based on sex and age groups, including 6–11 months, 12–23 months, 2–4 years, 5–9 years, 10–14 years and similar increments up to 95 years and older. When detailed age data were unavailable or sample sizes were small, broader age categories were used to ensure robust estimates.

To adjust for altitude-related variations in hemoglobin levels, altitude-adjusted data were included following the WHO adjustment formula<sup>30</sup>. However, no additional adjustments were made for factors

such as smoking status, hemoglobin sampling techniques or other analytical methods. This systematic approach ensured the reliability and accuracy of dietary iron deficiency estimates while accommodating regional and demographic variability.

### Modeling strategy

The burden of dietary iron deficiency was estimated using a two-stage process as follows:

1. Anemia envelope estimation. Hemoglobin distributions were modeled using Spatio-Temporal Gaussian Process Regression (ST-GPR) across 204 countries, disaggregated by age, sex, location and year. The ST-GPR model integrates covariates such as age-specific fertility rates, HIV prevalence and HAQI, allowing for refined estimates in regions with limited data. The model included random effects on location to account for regional variability in dietary iron deficiency prevalence. The variability of iron deficiency across anemia severity levels was not assumed to be constant; instead, severity-level-specific estimates were independently evaluated across different population subgroups.
2. Cause attribution for dietary iron deficiency. To estimate the contribution of dietary iron deficiency, the GBD study applied a globally systematic modeling process that integrates multiple high-quality datasets, such as the WHO Vitamin and Mineral Nutrition Information System, the Demographic and Health Survey, UNICEF Multiple Indicator Cluster Surveys and the National Health and Nutrition Examination Survey. Within this framework, dietary iron deficiency was estimated to account for 80.5% of residual anemia cases globally, reflecting its important role as a preventable cause of anemia. Counterfactual hemoglobin distributions, representing hypothetical levels without specific causes, were used to proportionally allocate anemia cases to dietary iron deficiency and other etiologies.

To estimate anemia prevalence attributable to specific causes, the analysis used modeled hemoglobin distributions for each location, year, age and sex, incorporating cause-specific prevalence and associated hemoglobin shifts. The estimated cause prevalence was multiplied by hemoglobin shifts to derive prevalence-weighted distribution shifts specific to each demographic and causal factor. Subsequently, mean hemoglobin estimates were adjusted using these weighted shifts, maintaining the original variance to re-estimate distributions. The difference between initial and counterfactual distributions across anemia severity levels was calculated to determine the prevalence attributable to each cause.

Unique hemoglobin shifts for dietary iron deficiency were derived from studies on iron fortification and supplementation intervention trials, applying a standardized shift of  $4.01 \text{ g l}^{-1}$ . This approach avoids relying on fixed proportions and, instead, dynamically evaluates dietary iron deficiency contributions across regions, age groups and levels of anemia severity. Variability in dietary contributions was captured by assessing unique counterfactual hemoglobin shifts for each anemia severity level, considering population-specific dietary intake patterns and regional factors. To ensure robustness, a minimum of 10% of anemia cases for each location, year, age and sex were allocated to residual causes. These residuals were proportionally distributed among dietary iron deficiency, other neglected tropical diseases, other infectious diseases and other hemoglobinopathies or hemolytic anemias, based on global age-specific and sex-specific proportions. Additionally, the GBD framework employs adjustments for demographic and regional factors, such as malaria prevalence, healthcare access and nutritional status, to refine hemoglobin distributions and anemia attribution. These adjustments ensure that estimates of dietary iron deficiency reflect regional and demographic variability, avoiding universal assumptions and enhancing the precision of burden estimates.

This proportional approach minimized confounding effects from chronic infections and metabolic disorders, allowing for a clear

distinction between anemia due to dietary iron deficiency and other causes<sup>30</sup> (Extended Data Fig. 8). To ensure consistency, residual causes were allocated a minimum of 10% of anemia cases, reflecting findings from large-scale nutritional surveys.

### Impact of inflammation and ferritin interpretation

The GBD model accounts for inflammatory conditions such as infections and chronic diseases that may complicate ferritin interpretation and dietary iron deficiency estimates. Although covariates such as C-reactive protein and albumin are not directly incorporated, the model includes proxy indicators of inflammatory burden, such as malaria incidence, HIV prevalence, and undernutrition metrics to inform hemoglobin shift estimates, minimizing the overestimation of dietary contributions in populations with high inflammatory burdens.

### Estimating anemia burden

We estimated the prevalence of mild, moderate and severe anemia across GBD locations, age groups, sexes and years<sup>30</sup>. Primary inputs for this estimation included mean hemoglobin concentration and its standard deviation<sup>30</sup>. Mean hemoglobin levels were modeled using an ST-GPR model to capture patterns and variations across populations and geographical areas. The ST-GPR model incorporated key covariates, such as age-specific fertility rate, HIV prevalence, child malnutrition indicators (for example, stunting and wasting), malaria incidence, healthcare access and quality index, modern contraceptive prevalence and genetic hemoglobin variants (hemoglobin C and S). These covariates enhanced hemoglobin-level prediction accuracy, particularly in data-limited areas<sup>2</sup>. The standard deviation of hemoglobin concentration was optimized based on the modeled mean and anemia prevalence by severity, allowing for hemoglobin distribution estimates tailored to each demographic group<sup>30</sup>.

### Estimating dietary iron deficiency burden

The estimation of dietary iron deficiency focused on the residual health burden remaining after accounting for explicitly modeled causes of anemia, such as malaria, menstrual disorders, gastrointestinal diseases and chronic kidney disease. The GBD cause attribution model then allocated the residual burden into four categories: dietary iron deficiency, neglected tropical diseases, infectious diseases and hemoglobinopathies or hemolytic anemias<sup>30</sup>. This step ensured that dietary iron deficiency was assessed within the narrower framework of residual causes, thereby excluding explicitly modeled causes of anemia and preventing the misattribution of other anemia etiologies to dietary iron deficiency.

To quantify dietary iron deficiency, 80.5% of the residual anemia burden was specifically attributed to this cause. This attribution was based on a standardized hemoglobin shift of  $4.01 \text{ g l}^{-1}$ , derived from robust evidence from iron supplementation and fortification trials. The remaining 19.5% of the residual burden was proportionally distributed among the other three residual categories to account for contributors not explicitly measured or modeled.

This dynamic approach evaluated dietary iron deficiency contributions across different severity levels, age groups, sexes and geographic regions, reflecting population-specific dietary patterns and regional influences<sup>33</sup>. By focusing on dietary iron deficiency as a preventable condition, the model underscores its distinct role in global health, separate from other anemia-related causes. The findings, summarized in Extended Data Fig. 8 and Supplementary Tables 3–5, highlight dietary iron deficiency as a key target for nutritional interventions, distinct from broader anemia-related etiologies.

### Calculation of YLDs and DALYs

DALYs were computed to quantify the overall burden of dietary iron deficiency. DALYs combine years of life lost due to premature death with YLDs, providing a comprehensive measure of health loss within a population<sup>33</sup>.

YLDs were calculated by multiplying the prevalence of sequelae for each disease and injury—categorized by cause, age, sex, location and year—by their respective disability weights<sup>2</sup>. For dietary iron deficiency, disability weights were assigned based on anemia severity: mild anemia (0.004), moderate anemia (0.052), and severe anemia (0.149)<sup>34</sup>. This method captures the varying impact of dietary iron deficiency across severity levels. Notably, the low disability weight for mild anemia reflects its minimal contribution to overall YLDs compared to moderate and severe cases. This approach captures the varying impact of dietary iron deficiency across severity levels, reflecting both mild anemia's low disability weight and its cumulative impact across large populations. By quantifying preventable cases of dietary iron deficiency, this method ensures consistency with established GBD guidelines while providing actionable insights into targeted interventions.

The YLD and DALY calculations adhered to established GBD guidelines, ensuring consistency across global and regional populations. By summing YLDs attributable to dietary iron deficiency, this approach provides a robust estimate of the health burden directly linked to inadequate dietary iron intake.

### Uncertainty

Uncertainty was incorporated at every stage of the estimation process by random sampling from possible value ranges for each estimate<sup>2</sup>. When results were combined across different categories (for example, SDI, geography or age), each sample was treated independently. The final uncertainty interval for each result was determined using the 2.5th and 97.5th percentiles of the draws. In addition to incorporating random sampling, non-sampling variance was calculated using residuals from hierarchical models across geographic levels. For regions with sparse data, variance adjustments were applied to enhance the robustness of the estimates. Bias adjustments were implemented through network analysis, leveraging indirect comparisons to strengthen estimates where direct data comparisons were unavailable. This comprehensive approach accommodates variability across diverse populations and geographies, improving the reliability of dietary iron deficiency estimates.

### Error variance and uncertainty

Non-sampling variance was incorporated into the estimation process by analyzing weighted residuals from hierarchical models across geographic levels. This step accounts for variance even when sample sizes are small, improving estimate reliability. Error variance in the normal and logit-transformed spaces was calculated for hemoglobin levels, with variance adjustments applied where sample size information was unavailable. Uncertainty intervals for all estimates were derived from 1,000 random samples per estimate, with final 95% uncertainty intervals based on the 2.5th and 97.5th percentiles. This approach ensured robust uncertainty estimates, accommodating variability across age, sex and location.

### Data adjustments—crosswalking

Crosswalking is the process of adjusting data to account for known biases<sup>34</sup>. An observation is considered biased if it consistently differs from the standard GBD definition of the modeled parameter. Examples include measures of disease incidence that are self-reported rather than doctor-diagnosed or diagnostic tests that have lower sensitivity or specificity compared to the gold standard diagnostic method. If the difference between an alternative measurement method and the GBD definition is consistent and systematic, it can be modeled using covariates, allowing us to predict the necessary adjustment for a given alternative or non-standard observation. This process enables GBD models to incorporate data from a wider array of sources.

### Data adjustments—bias adjustment for alternative case definitions and study methods

In GBD 2021, we continued adjusting non-fatal and risk exposure data for different case definitions or study methods, a practice started in

GBD 2019. These adjustments were made before using ST-GPR, ensuring consistent data inputs and converting data for both sexes into male and female equivalents. We identified and compared alternative and reference definitions within and between studies, allowing a 5-year difference in between-study comparisons. We quantified bias by calculating differences between matched pairs of alternative and reference observations, using these as dependent variables in a mixed-effect meta-regression model. Covariates were chosen based on systematic differences, and adjustments were applied even without statistical significance if conceptual bias was likely. An open-source Python package (ihmeuw-msca, 2023) was developed to assist with these adjustments, increasing the variance of non-standard data points and reducing their influence in further modeling.

### Data adjustments—example bias adjustment calculation

To adjust for bias in data sources measuring prevalence with non-standard case definitions, we matched pairs of alternative and reference observations by age, sex, location and time period, calculating logit-scale differences to account for bias. If values were zero, data were aggregated across age groups until they became non-zero. Standard errors were computed using the delta method. Differences were modeled in a mixed-effects meta-regression with age and sex as covariates to predict bias adjustments. Adjustments were applied by subtracting the logit-space adjustment factor and using the inverse logit transformation. Uncertainty included the original observation's uncertainty, the predicted adjustment's posterior distribution and random intercepts from the model, with variances summed and transformed back to natural units.

### Data adjustments—network analysis

When multiple alternative case definitions or study methods were present, we used network analysis to utilize additional information from indirect comparisons. For example, if A is the reference and B and C are alternatives, a direct comparison is C versus A, whereas an indirect comparison combines A versus B and B versus C. This method enhances estimates by including more data. Implementing network analysis involves constructing a design matrix for the mixed-effects meta-regression model. If case definitions have subcomponents (for example, symptoms and recall periods), sparse data can make direct and indirect comparisons difficult. In such cases, we assume multiplicative effects across dimensions and use dummy variables to encode these effects. The open-source Python package (ihmeuw-msca, 2023) facilitates this process by automating the design matrix creation and accommodating multiple alternative definitions and covariates.

### Data adjustments—elevation adjustment

Hemoglobin concentration exhibits a positive correlation with elevation, representing a physiological adaptation to decreased ambient oxygen levels, thereby ensuring adequate oxygen delivery throughout the body. Below 1,000 m, the impact on hemoglobin appears negligible. However, previous research suggests an exponential relationship between elevation and hemoglobin levels, as reflected in the WHO-recommended formula for hemoglobin adjustment:

$$\Delta\text{Hb} = -0.32 \times (\text{elevation in meters} \times 0.0033) + 0.22 \times (\text{elevation in meters} \times 0.0033)^2$$

In this analytical approach, GBD modeling used survey-reported data that were either elevation adjusted or both elevation adjusted and smoking adjusted, without further modification. For individual-level data presenting unadjusted hemoglobin values but including elevation information, the equation was applied to make necessary adjustments. Further studies are necessary to test alternative elevation adjustment methodologies. In the absence of smoking-adjusted data, no additional modifications were implemented in the GBD 2021 analysis.

This methodological decision acknowledges the limitations of available data while maintaining consistency across the dataset.

### ST-GPR modeling

GPR is a flexible statistical method used when sufficient data exists to track complex changes over time. This modeling technique is designed to detect signals in noisy data. It also functions as a powerful tool for interpolating nonlinear trends. Unlike traditional linear models that assume definitive functional forms for underlying trends, GPR considers the trend of interest as following a Gaussian process. This process is characterized by two components: a mean function  $m(\cdot)$  and a covariance function  $\text{Cov}(\cdot)$ . As an example,  $p_{c,a,s,t}$  denotes the observed data in normal, log, or logit space, observed in country  $c$ , for age group  $a$  and sex  $s$  at time  $t$ :

$$(p_{c,a,s,t}) = g_{c,a,s}(t) + \epsilon_{c,a,s,t}$$

where

$$\epsilon_{c,a,s,t} \sim \text{Normal}(0, \sigma_p^2),$$

$$g_{c,a,s}(t) \sim \text{GP}(m_{c,a,s}(t), \text{Cov}(g_{c,a,s}(t))).$$

The calculation of mean and covariance functions,  $m_{c,a,s}(t)$  and  $\text{Cov}(g_{c,a,s}(t))$ , alongside a comprehensive explanation of error variance ( $\sigma_p^2$ ), is outlined in the following section.

### Estimating mean functions

Mean functions were calculated through a two-phase process.  $m_{c,a,s}(t)$  can be formulated, depending on the exposure transformation, as:

$$\log(p_{c,a,s}(t)) = X_{c,a,s}\beta + h(r_{c,a,s,t})$$

$$\text{logit}(p_{c,a,s}(t)) = X_{c,a,s}\beta + h(r_{c,a,s,t})$$

$$p_{c,a,s}(t) = X_{c,a,s}\beta + h(r_{c,a,s,t})$$

where  $X\beta$  represents the aggregate of hierarchical linear mixed-effects regression components, encompassing the intercept and covariate-coefficient products. The models used hierarchical linear mixed-effects regressions with random intercepts at various geographic levels. These random intercepts were applied during fitting but were excluded from predictions. An ensemble model combined these regressions. The latter part of the equation,  $h(r_{c,a,s,t})$ , functions as a residual smoothing mechanism, where  $r_{c,a,s,t}$  stems from the initial ensemble linear model. Although the linear element captures overall exposure trends over time, considerable data variability often remains unaccounted for. To resolve this, a locally weighted polynomial regression function,  $h(r_{c,a,s,t})$ , was applied. This approach systematically estimates residual variability by leveraging patterns across time, age and space—the spatiotemporal aspect of ST-GPR. The time adjustment parameter,  $\lambda$ , aims to borrow strength from adjacent timepoints, recognizing that exposure in a given year correlates strongly with the previous year but less so with earlier years. The age adjustment parameter,  $\omega$ , uses data from proximate age groups. The space adjustment parameter,  $\xi$ , aims to borrow strength across geographic hierarchies. Spatial and temporal weights merge into a unified space-time weight, allowing spatial weight for a specific point  $r_{c,a,s,t}$  to vary based on data availability at each time  $t$  and location-level  $l$  within the hierarchy.

The final weight  $w_{c,a,s,t}$  is assigned to observation  $r_{c,a,s,t}$  relative to a focal observation  $r_{c_0,a_0,s_0,t_0}$ . Initially, a temporal weight  $t.w_{c,a,s,t}$  was created for time-based smoothing, calculated using the scaled temporal distance between observations:

$$t.w_{c,a,s,t} = \frac{1}{e^{\lambda|t-t_0|}}$$

Subsequently, a spatial weight was developed for geographic smoothing. A geospatial relationship was established by categorizing data according to the GBD location hierarchy. The parameter  $\zeta$  functions as a scalar for each data point, reflecting its proximity to the target location:

$$t.w_{c,a,s,t} = \zeta^{|c-c_0|}$$

For example, estimating a country would use the following weighting scheme:

- Country data:  $\zeta^0 = 1$
- Regional data not from the country being estimated:  $\zeta^1$
- Data from other regions in the same super-region:  $\xi^2$
- Global data from other super-regions:  $\zeta^3$

In the spatial weighting framework,  $\zeta$  typically ranges from 0.001 to 0.2. This parameter indicates how much regional data are down-weighted relative to country-specific data for a given estimate. For instance, with  $\zeta = 0.01$  and a data point  $r_{c,a,s,t}$ , another point from the same region but different country would receive  $\frac{1}{100}$  the weight of an in-country data point.

Given a normalization constant,

$$K_i = \sum_{cc} s.w_{c,t} \times t.w_{c,t} + \sum_{cCR} s.w_{c,t} \times t.w_{c,t} + \sum_{ccSR} s.w_{c,t} \times t.w_{c,t}$$

the final space-time weight would then equal

$$w'_{c,a,s,t} = \frac{s.w_{c,t} \times t.w_{c,t}}{K_i}$$

Lastly, a weight  $w''_{c,a,s,t}$  was computed for age smoothing, based on the age difference between two observations. For a point between the age  $a$  of the observation  $r_{c,a,s,t}$  and a focal observation  $r_{c_0,a_0,s_0,t_0}$ , the weight is defined as follows:

$$w''_{c,a,s,t} = \frac{1}{e^{|\omega|a-a_0|}}$$

The final weights are calculated by multiplying space-time weights with age weights and then normalizing to ensure all weights for a specific time period  $t$  sum to 1. A comprehensive derivation of weights for each category, assuming a country-level estimation, is as follows:

1) When the observation  $r_{c,t}$  originates from the identical country  $c_0$  as the focal observation  $r_{c_0,t_0}$ :

$$w_{c,a,s,t} = \frac{(w'_{c,a,s,t} w''_{c,a,s,t})}{\sum_{c=c_0} (w'_{c,a,s,t} w''_{c,a,s,t})} \quad \forall c = c_0$$

2) If observation  $r_{c,t}$  comes from a different country than focal observation  $r_{c_0,t_0}$ , but both belong to the same region  $R$ :

$$w_{c,a,s,t} = \frac{(w'_{c,a,s,t} w''_{c,a,s,t})}{\sum_{c \neq c_0} (w'_{c,a,s,t} w''_{c,a,s,t})} \quad \forall c \neq c_0 \cap R[c] = R[c_0]$$

3) When observation  $r_{c,t}$  is from the same super-region  $SR$  but differs in both country  $c_0$  and region  $R[c_0]$  from the focal observation  $r_{c_0,t_0}$ :

$$w_{c,a,s,t} = \frac{(w'_{c,a,s,t} w''_{c,a,s,t})}{\sum_{c \neq c_0} (w'_{c,a,s,t} w''_{c,a,s,t})} \quad \forall c \neq c_0 \cap R[c] \neq R[c_0] \cap SR[c] = SR[c_0]$$

4) When observation  $r_{c,t}$  originates from a different super-region than focal observation  $r_{c_0,c_0}$  (encompassing all remaining data not yet assigned a weight):

$$w_{c,a,s,t} = \frac{(w'_{c,a,s,t} w''_{c,a,s,t})}{\sum_{c \neq c_0} (w'_{c,a,s,t} w''_{c,a,s,t})}$$

$$\forall c \neq c_0 \cap R[c] \neq R[c_0] \cap SR[c] \neq SR[c_0]$$

The final weights underwent normalization, ensuring that the total sum of weights across age, time and geographic hierarchy for each reference group equaled 1.

### Estimating error variance

$\sigma_p^2$  denotes error variance in normal or transformed space, encompassing sampling variance of estimates and prediction error from cross-walks. The variance was systematically imputed when data extraction lacked uncertainty measures. For available sample sizes, missing ones were imputed using the 5th percentile of existing samples. Missing variances were calculated as  $\sigma_p^2 = \frac{p(1-p)}{n}$  for proportions or predicted via regression for continuous values. When sample sizes were completely absent, the 95th percentile of available variances at the most granular geographic level served as imputation. For proportions where  $p \times n$  or  $(1-p) \times n$  is less than 20, the variance was replaced using the Wilson interval score method.

For exposures modeled with log transformation, the error variance was converted to log space using the delta method approximation:

$$\sigma_p^2 \cong \frac{\sigma_{p'}^2}{p_{c,a,s,t}^2}$$

where  $\sigma_{p'}^2$  denotes the error variance in normal space. For exposures modeled with logit transformation, the error variance was converted to logit space using the delta method approximation as follows:

$$\sigma_p^2 \cong \frac{\sigma_{p'}^2}{(p_{c,a,s,t} \times (1-p_{c,a,s,t}))^2}$$

Before applying GPR, an estimate of non-sampling variance was incorporated into the error variance. These calculations were performed on normal-space variances. Non-sampling variance was derived from the variance of inverse-variance weighted residuals from space-time estimates at each location-level hierarchy. For levels with fewer than 10 data points, the non-sampling variance was substituted with that from the next higher geographic level containing more than 10 data points.

### Estimating the covariance function

The final input into GPR is the covariance function, determining trend shape and distribution. The Matern–Euclidian covariance function was selected for its versatility in modeling diverse trends with different smoothness levels. This function is defined as:

$$M(t, t') = \sigma^2 \frac{2^{1-\nu}}{\Gamma(\nu)} \left( \frac{d(t, t') \sqrt{2\nu}}{l} \right)^\nu K_\nu \left( \frac{d(t, t') \sqrt{2\nu}}{l} \right)$$

where  $d(\cdot)$  represents a distance measure. The hyperparameters  $\sigma^2$ ,  $\nu$ ,  $l$  and  $K_\nu$  are defined as key aspects of the covariance function. Specifically,  $\sigma^2$  denotes marginal variance;  $\nu$  determines function smoothness and differentiability;  $l$  represents the length scale (indicating when two points become uncorrelated); and  $K_\nu$  is the Bessel function.  $\sigma^2$  was approximated using the normalized median absolute deviation (MADN) ( $r_c$ ) of the difference, which is the normalized absolute deviation of the difference between first-stage linear regression and second-stage spatiotemporal smoothing estimates for each country.

The mean of these country-level MADN estimates was calculated for nations with more than 10 years of data, ensuring robust information on model uncertainty. All models employed a parameter specification of  $\nu = 2$ .

### Covariates

The modeling approach for dietary iron deficiency employed ST-GPR to estimate mean hemoglobin levels and anemia prevalence across various severities. This multi-step modeling process generated comprehensive estimates for each combination of location, year, age, and sex within the GBD framework. Covariates included factors known to impact hemoglobin levels and anemia prevalence, allowing the model to adjust for demographic, socioeconomic and health-related influences on iron deficiency.

1. Step 1: Ensemble linear mixed-effects regression. The initial phase used ensemble linear mixed-effects regression to account for potential predictive covariates drawn from the GBD study database. These covariates were tested in various combinations with nested random intercepts applied at different geographic levels. This approach allowed the model to capture hierarchical variability by location, improving accuracy in regions with sparse data. The covariate models with the lowest out-of-sample root mean squared error (RMSE) were selected and averaged to produce baseline estimates.
2. Step 2: Spatiotemporal smoothing of residuals. After the initial regression, residuals (differences between the observed data points and the model estimates) were smoothed over space, age and time. This spatiotemporal smoothing process enhanced the precision of the initial estimates by utilizing patterns in adjacent time points, neighboring age groups and nearby geographical areas. This stage drew strength across data points, filling gaps and reducing variability where data coverage was limited.
3. Step 3: Gaussian process regression refinement. In the final step, GPR was applied to refine the smoothed estimates further. GPR is particularly effective for tracking complex, nonlinear trends over time, as it adapts to regional data patterns without imposing a rigid trend form. This refinement produced robust estimates of mean hemoglobin and anemia prevalence across diverse population groups and settings.

Throughout the modeling process, mean hemoglobin data were log transformed, whereas anemia prevalence data were logit transformed to enhance normality and stabilize variance in the data. Covariates were carefully selected based on both their statistical significance and their anticipated influence on hemoglobin levels and anemia prevalence, ensuring that each covariate aligned with established biological or socioeconomic determinants of dietary iron deficiency. Supplementary Table 2 outlines the specific covariates used in the model, along with their expected direction of influence on mean hemoglobin and anemia prevalence. Covariate-specific insights include:

1. Age-specific fertility rate and HIV prevalence are associated with increased anemia prevalence and decreased hemoglobin levels due to higher physiological demands and the immune impact of HIV, respectively.
2. Child underweight and wasting indicate malnutrition, impacting growth and increasing susceptibility to iron deficiency.
3. Malaria incidence contributes to anemia by causing hemolysis, which disrupts iron homeostasis, and hemoglobin C and S traits represent genetic factors impacting hemoglobin levels, especially in regions with high sickle cell prevalence.
4. SDI serves as a broad indicator of socioeconomic development, where higher SDI is typically linked to improved nutrition, higher hemoglobin levels and lower anemia prevalence.

5. HAQI and modern contraception prevalence reflect access to health services and reproductive care, which impact maternal anemia risk.

This carefully curated set of covariates allowed the ST-GPR model to differentiate trends in dietary iron deficiency prevalence from changes in broader anemia prevalence driven by other health or environmental factors. This robust covariate inclusion strategy supports the validity and applicability of the model's predictions across different demographic and geographic contexts.

### Prediction using GPR

Integration over  $g_{c,t}(t_*)$  was performed to predict a complete time series for country  $c$ , age  $a$ , sex  $s$  and prediction time  $t_*$  as follows:

$$p_{c,a,s}(t_*) \sim N(m_{c,a,s,t}(t_*), \sigma_p^2 I + \text{Cov}(g_{c,a,s,t}(t_*)))$$

For each country and indicator, 1,000 random samples were drawn from the specified distributions. The final estimated mean for each country was calculated as the average of these draws. Additionally, 95% uncertainty intervals were determined using the 2.5th and 97.5th percentiles of the sample distribution.

### Subnational scaling and aggregation

Internal consistency between national and subnational estimates was maintained through two methods, depending on data coverage. When national data coverage surpassed subnational coverage, subnational estimates were adjusted using population-weighted scaling to align with national estimates. When subnational data coverage was superior, national estimates were derived using population-weighted aggregation of subnational data. This approach was applied across age, sex and time dimensions for each country and risk factor. Additionally, scaling could be performed in logit space, ensuring that subnational proportion estimates remained below 1 after adjustment to align with national levels.

### Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

### Data availability

The findings from this study were produced using data available in public online repositories or in the published literature; data that are publicly available upon reasonable request from the data provider; and data that are not publicly available due to restrictions by the data provider and that were used under license for the current study. Details on data sources can be found on the Global Health Data Exchange website, including information about the data provider and links to where the data can be accessed or requested (where available). Citations and metadata for all input sources used in this analysis are available for download at <https://ghdx.healthdata.org/gbd-2021/sources> (to access all sources, select non-fatal health outcomes as the component and dietary iron deficiency as the cause).

### Code availability

Our study follows the Guidelines for Accurate and Transparent Health Estimate Reporting (GATHER; Supplementary Table 1). All code used for this analysis is publicly available online at [https://github.com/ihmeuw/anemia\\_gbd2021](https://github.com/ihmeuw/anemia_gbd2021).

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### Author contributions

Conceptualization and design: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; methodology: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; data acquisition: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; statistical analysis and data curation: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; validation: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; data interpretation: S.L., Y.S., J.H., M.S.K., J.I.S., D.K.Y. and N.J.K.; visualization: S.L., Y.S., J.H. and M.S.K.; managing the estimation or publications process: N.J.K., M.S.K. and J.I.S.; writing—original draft preparation: S.L., Y.S., J.H. and M.S.K.; writing—review and editing: all authors provided critical revision to the paper; supervision: J.I.S., D.K.Y. and N.J.K.; project administration: J.I.S., D.K.Y. and N.J.K.; funding acquisition: J.I.S., D.K.Y. and N.J.K. N.J.K. is the senior author. Contributions by the GBD 2021 Dietary Iron Deficiency Collaborators are described in Supplementary Note 1.

### Competing interests

N.J.K. reports grants or contracts from the Bill & Melinda Gates Foundations as well as grant funding for anemia-related research. N.J.K. also reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Bristol Myers Squibb (presentation on GBD 2021 findings for anemia and dietary iron deficiency), outside the submitted work. Competing interests for the GBD 2021 Dietary Iron Deficiency Collaborators are listed in Supplementary Note 2.

### Additional information

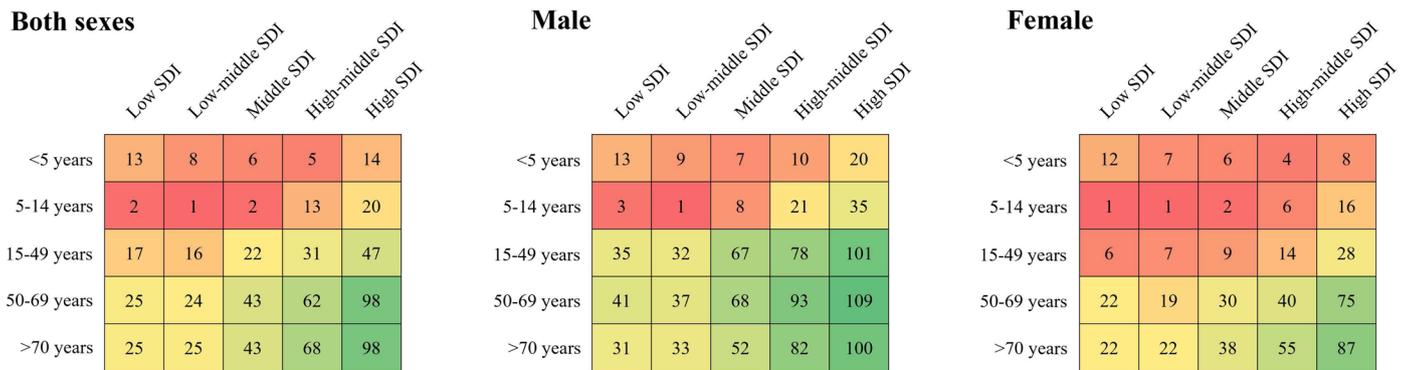
**Extended data** is available for this paper at <https://doi.org/10.1038/s41591-025-03624-8>.

**Supplementary information** The online version contains supplementary material available at <https://doi.org/10.1038/s41591-025-03624-8>.

**Correspondence and requests for materials** should be addressed to Jae Il Shin or Dong Keon Yon.

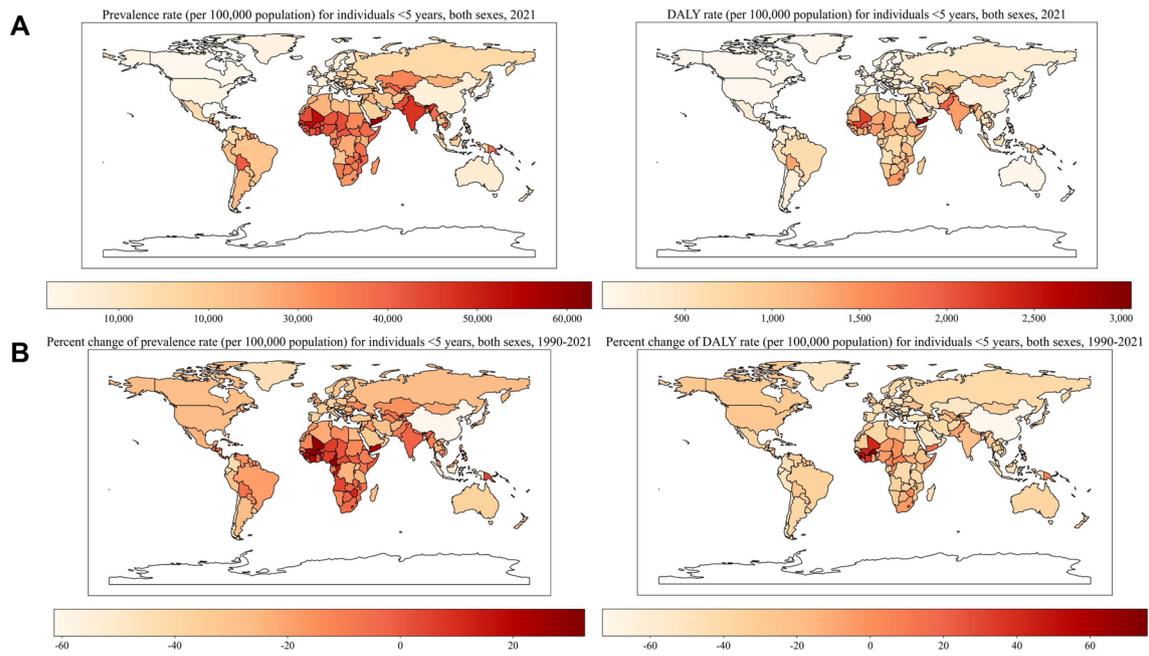
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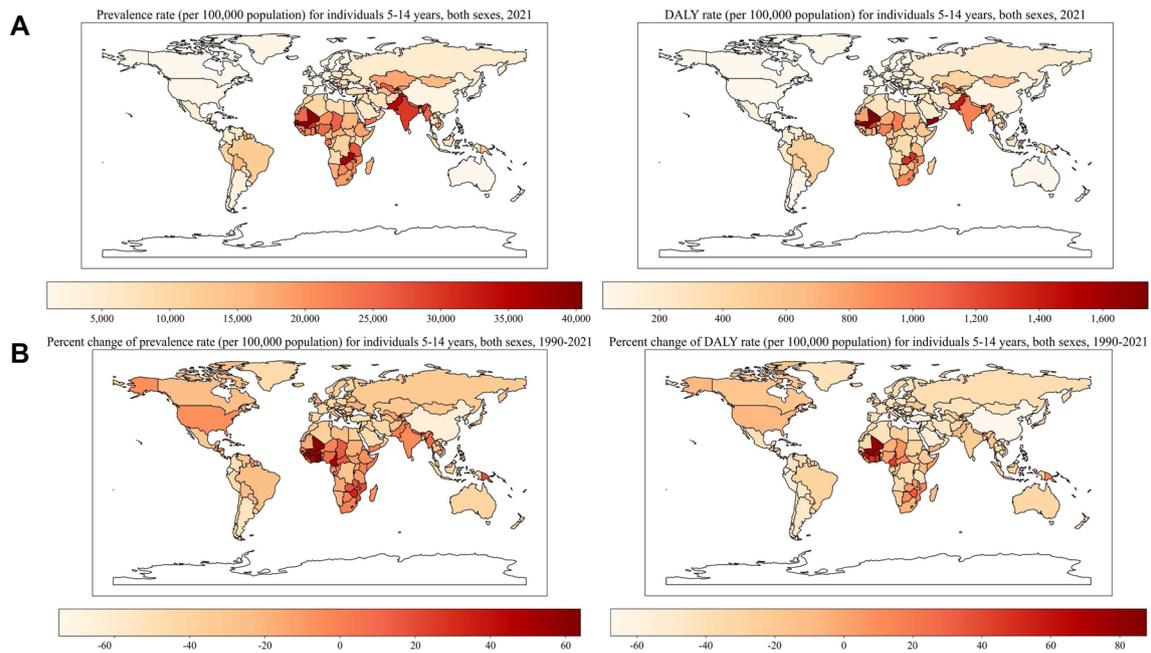
**Extended Data Fig. 1 | Global rank of dietary iron deficiency in DALYs rate by sex, age group, and SDI.** Global ranks of dietary iron deficiency in DALYs per 100,000 population are displayed by sex, age group, and SDI quintile. The three panels represent data for both sexes (left), males (middle), and females (right).

Rows correspond to age groups (70 years), while columns represent SDI quintiles from low to high. Each cell contains the global rank of dietary iron deficiency for the corresponding subgroup, with color gradients reflecting the rank, ranging from red (higher rank) to green (lower rank).



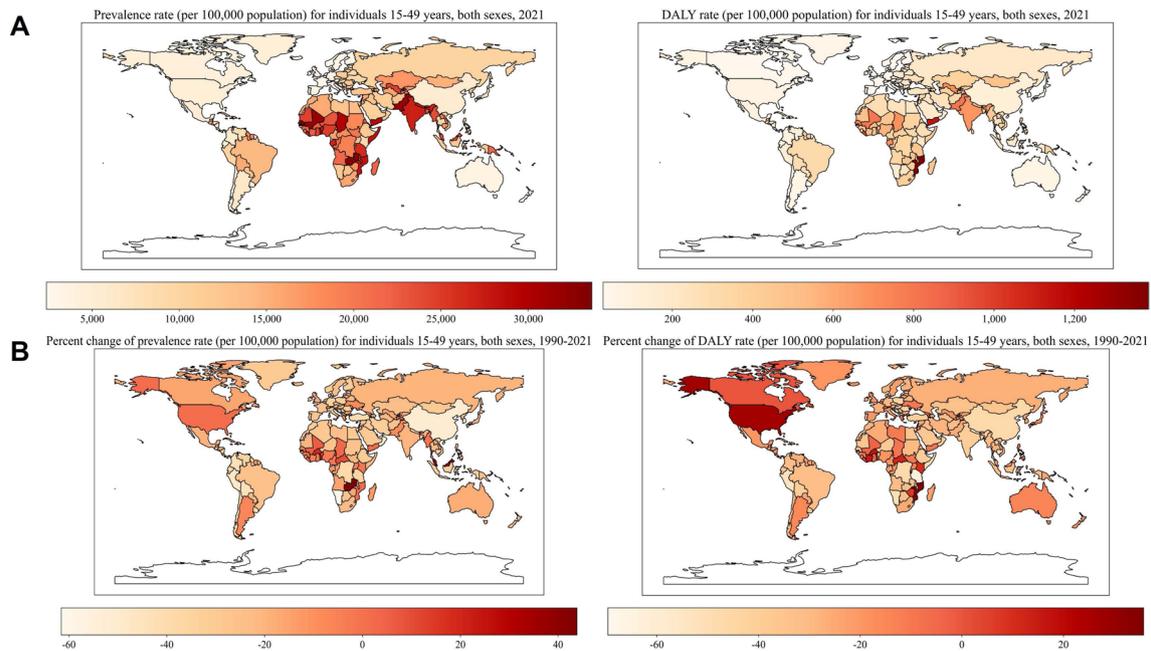
**Extended Data Fig. 2 | Global distributions for dietary iron deficiency in individuals under 5 years.** Global maps display the prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency among individuals under 5 years of age, both sexes, in 2021 (**a**). Global maps show the percent change in

prevalence rate and DALY rate (per 100,000 population) for the same population group from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



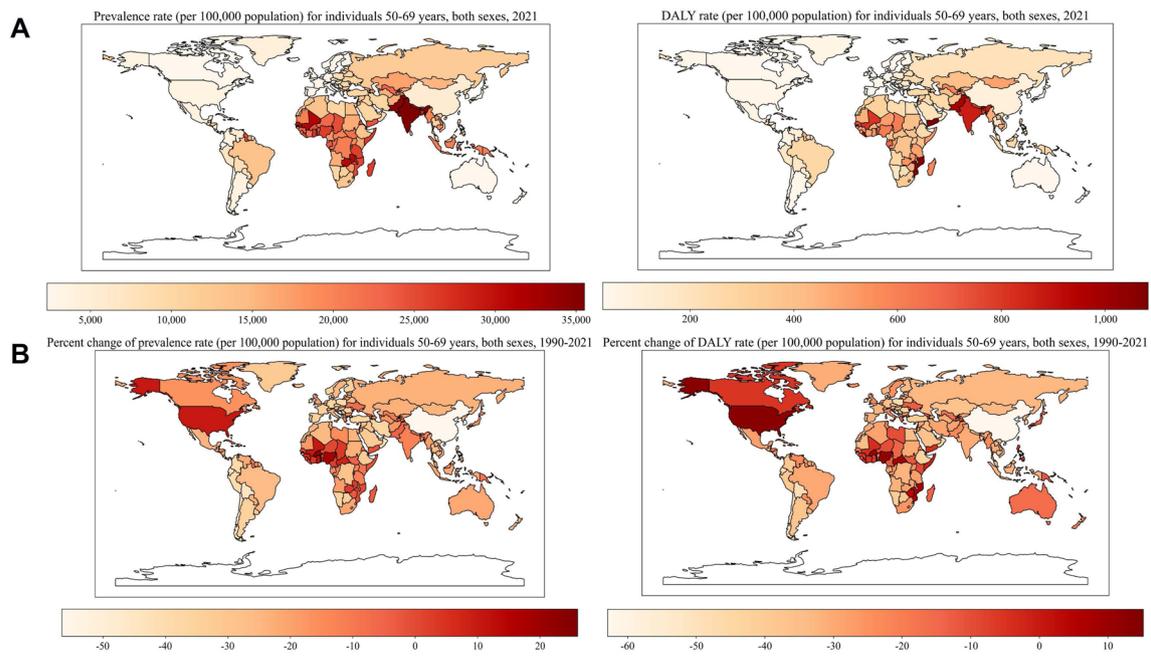
**Extended Data Fig. 3 | Global distributions for dietary iron deficiency in individuals aged 5–14 years.** Global maps display the prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency among individuals aged 5–14 years, both sexes, in 2021 (**a**). Global maps show the percent change in

prevalence rate and DALY rate (per 100,000 population) for the same population group from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



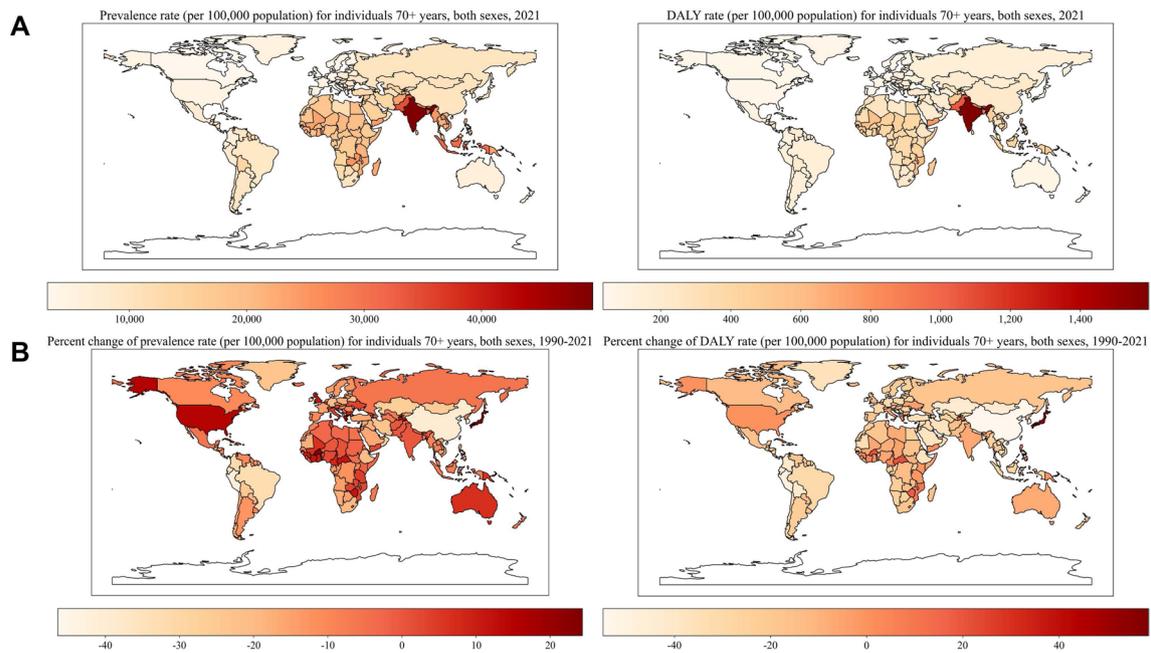
**Extended Data Fig. 4 | Global distributions for dietary iron deficiency in individuals aged 15–49 years.** Global maps display the prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency among individuals aged 15–49 years, both sexes, in 2021 (**a**). Global maps show the percent change in

prevalence rate and DALY rate (per 100,000 population) for the same population group from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



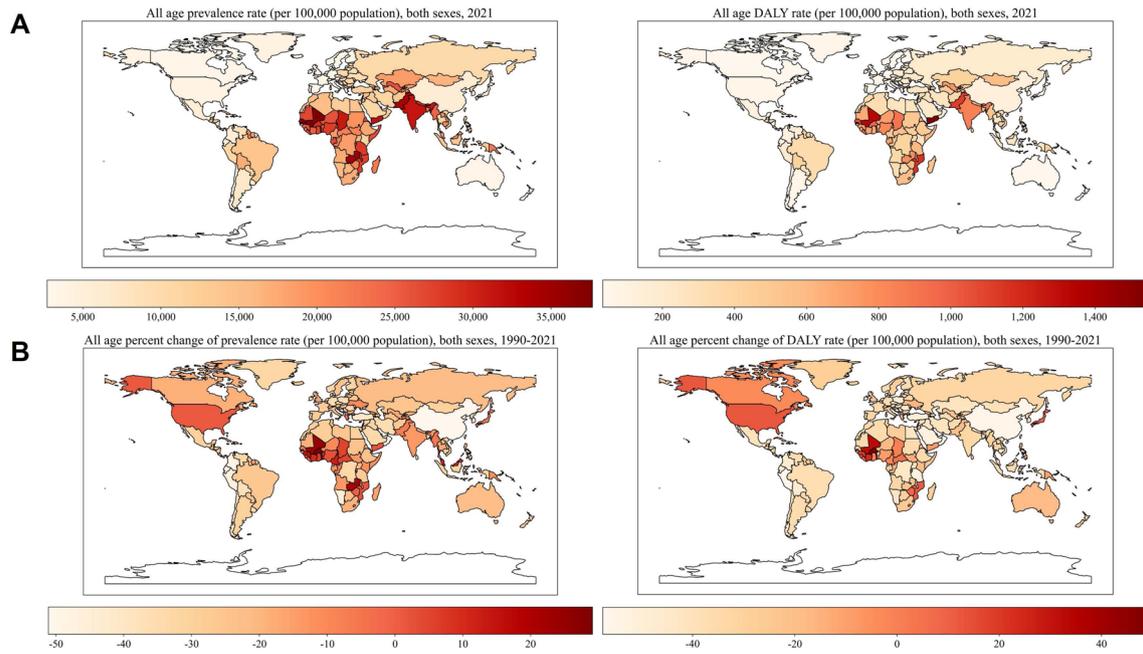
**Extended Data Fig. 5 | Global distributions for dietary iron deficiency in individuals aged 50–69 years.** Global maps display the prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency among individuals aged 50–69 years, both sexes, in 2021 (**a**). Global maps show the

percent change in prevalence rate and DALY rate (per 100,000 population) for the same population group from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



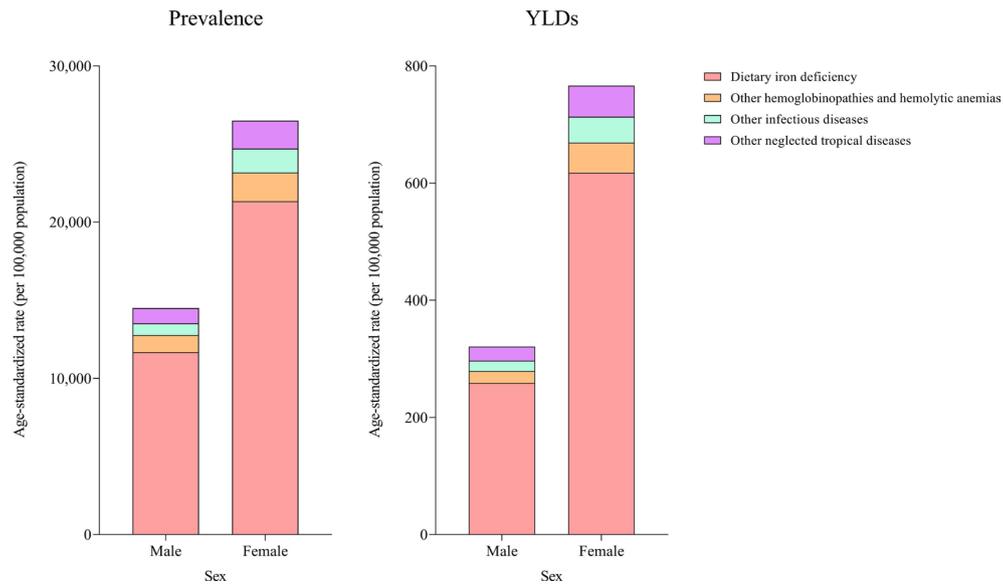
**Extended Data Fig. 6 | Global distributions for dietary iron deficiency in individuals aged >70 years.** Global maps display the prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency among individuals aged > 70 years, both sexes, in 2021 (**a**). Global maps show the percent change in

prevalence rate and DALY rate (per 100,000 population) for the same population group from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



**Extended Data Fig. 7 | Global distributions for dietary iron deficiency across all age groups.** Global maps display the all-age prevalence rate and DALY rate (per 100,000 population) for dietary iron deficiency in both sexes in 2021 (**a**). Global maps show the all-age percent change in prevalence rate and DALY rate

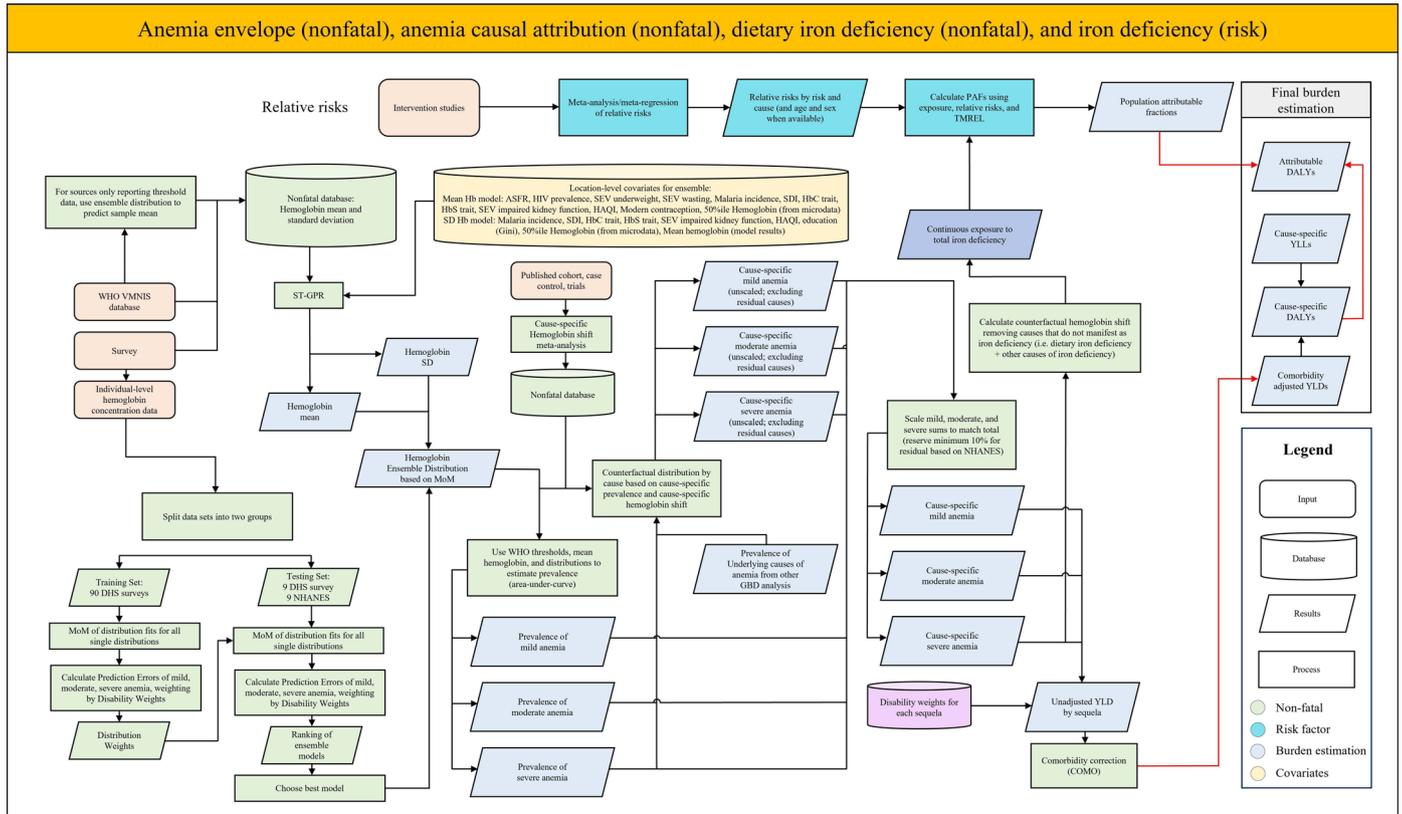
(per 100,000 population) for dietary iron deficiency in both sexes from 1990 to 2021 (**b**). The maps use color gradients to illustrate geographical variations, with darker shades representing higher values in (**a**) or larger percent changes in (**b**).



**Extended Data Fig. 8 | Age-standardized prevalence and YLDs due to anemia causes by sex, 2021.**

Age-standardized rates of prevalence and YLDs due to anemia causes are displayed by sex for 2021. Dietary iron deficiency (pink) constitutes the largest segment of both prevalence and YLDs for males and

females, followed by contributions from hemoglobinopathies and hemolytic anemias (orange), other infectious diseases (green), and neglected tropical diseases (purple). The bars, color-coded for specific causes, illustrate the relative proportions attributed to each anemia cause across sexes.



**Extended Data Fig. 9 | Flow chart of dietary iron deficiency.** The methodological framework outlines the estimation process for the burden of dietary iron deficiency, anemia (nonfatal), and their causal attributions. It integrates data inputs such as individual hemoglobin levels, and survey data, utilizing ST-GPR to model hemoglobin mean and standard deviation. Cause-specific prevalence and hemoglobin shifts are derived for mild, moderate, and

severe anemia, incorporating counterfactual distributions to attribute cases specifically to dietary iron deficiency. Disability weights are applied to calculate YLDs and DALYs, while comorbidity corrections refine the estimates. Relative risks, population-attributable fractions, and covariates are combined to provide a structured pathway from raw data to final burden estimation within the GBD framework.

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No primary data collection was carried out for these analyses. Relevant data from population surveys, published studies, and government reports were extracted by a reviewer using a data collection. The findings of this study are based on data from multiple sources, including public online repositories, data available on request, and restricted data used under license. Comprehensive information on all data sources, including provider details and access instructions where applicable, is

available through the Global Health Data Exchange GBD 2021 website <https://ghdx.healthdata.org/gbd-2021>.

This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations (Table S1). All maps presented in this study are generated by the authors; no permissions are required for publication.

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Reporting on sex and gender	No primary data collection was carried out for this analysis, so the study does not involve human research participants.
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Recruitment	Not applicable.
Ethics oversight	This study was approved by the University of Washington IRB Committee.

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## Life sciences study design

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Sample size	The sample size used in the study model is defined as the population from all locations analyzed from 1990 to 2021. 204 countries and territories, categorized into 21 regions and seven broad super-regions. The population at the state, national, regional, super-regional, and global levels was estimated as part of the Global Burden of Disease Study 2021 and represents the global population based on various demographic characteristics such as age (6-11 months, 12-23 months, 2-4 years, 5-9 years, 10-14 years, and similar increments up to 95 years and older), sex, and regions. Detailed methods are described in <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00757-8/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)00757-8/fulltext</a> .
Data exclusions	We carefully evaluated all data sources for inclusion in our study. Sources were excluded if they lacked necessary survey weight factors or crucial demographic information such as sex or age variables. Additionally, we omitted data deemed unreliable, based on assessments by survey administrators or through our own detailed examination. This careful selection process ensured the quality and completeness of the information used in our analysis.
Replication	This study is an observational study based on several years of survey and report data and is, in principle, replicable. However, due to the time required to extract, process, geo-locate all data, and run the statistical models, an explicit replication analysis was not conducted.
Randomization	Randomization was not relevant to this study. This analysis is an observational mapping study and there were no experimental groups.
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