

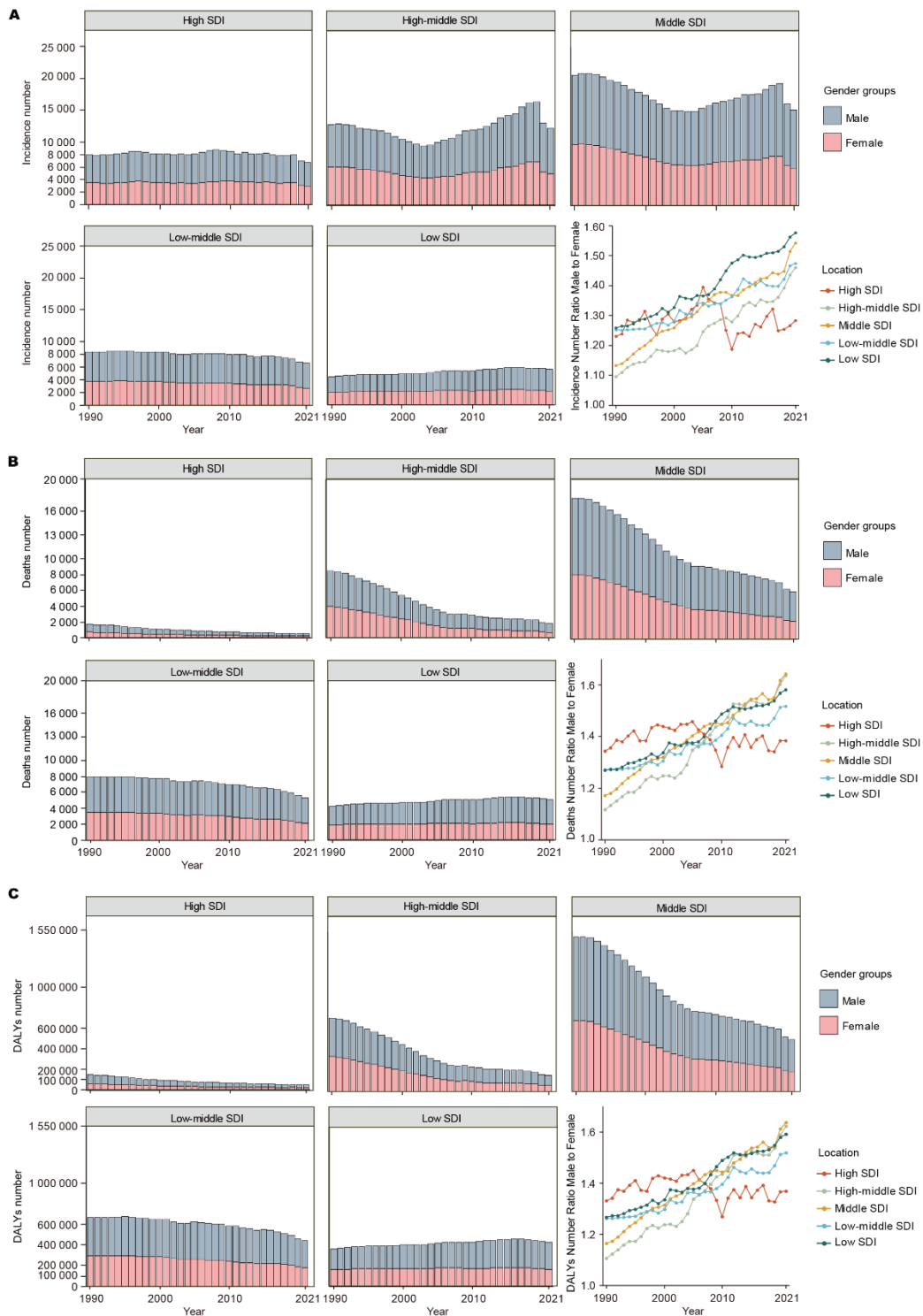
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Supplemental information

Global, regional, and national burden of acute lymphoblastic leukemia in children: Epidemiological trends analysis from 1990 to 2021

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Figure S1: Trends in incidence, deaths, and DALYs of childhood ALL by gender and gender ratio across SDI regions (1990-2021), related to Figure 2



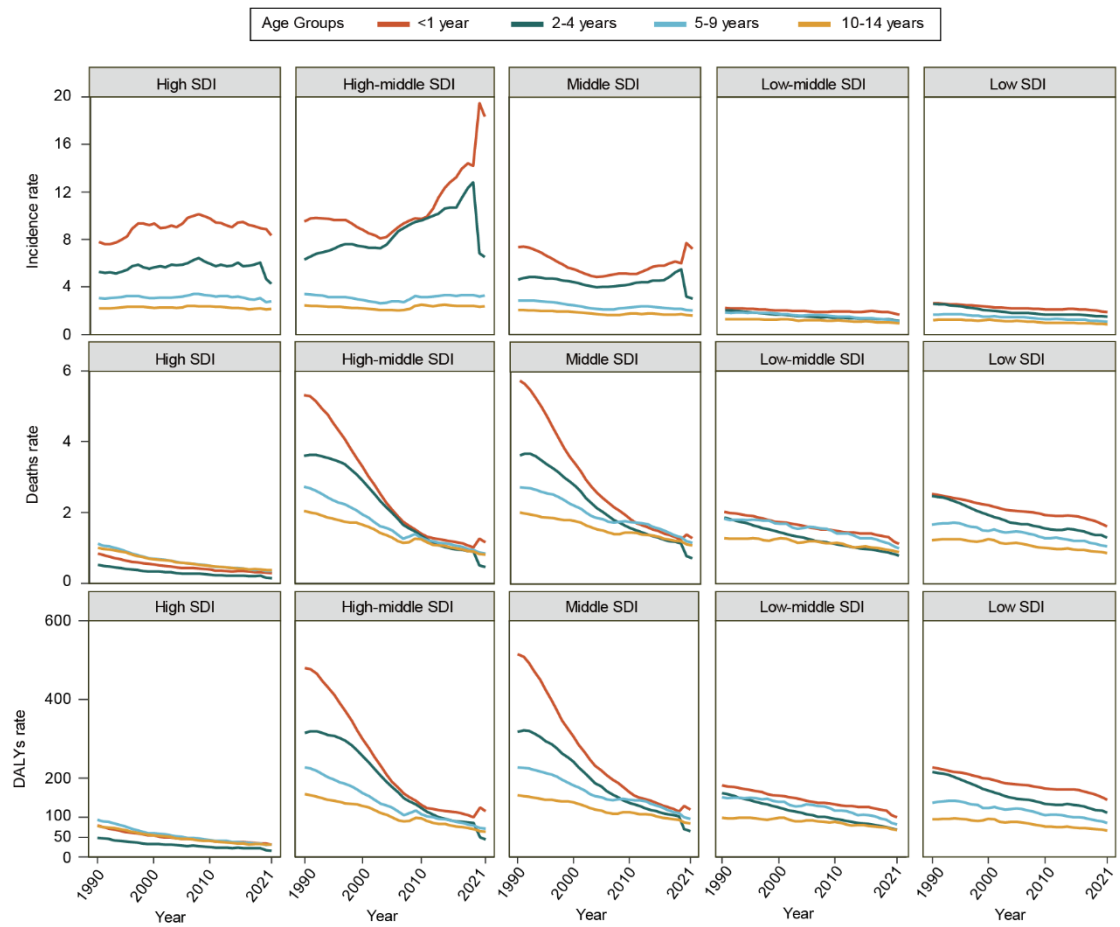
A: Trends in incidence number.

B: Trends in deaths number.

C: Trends in DALYs number.

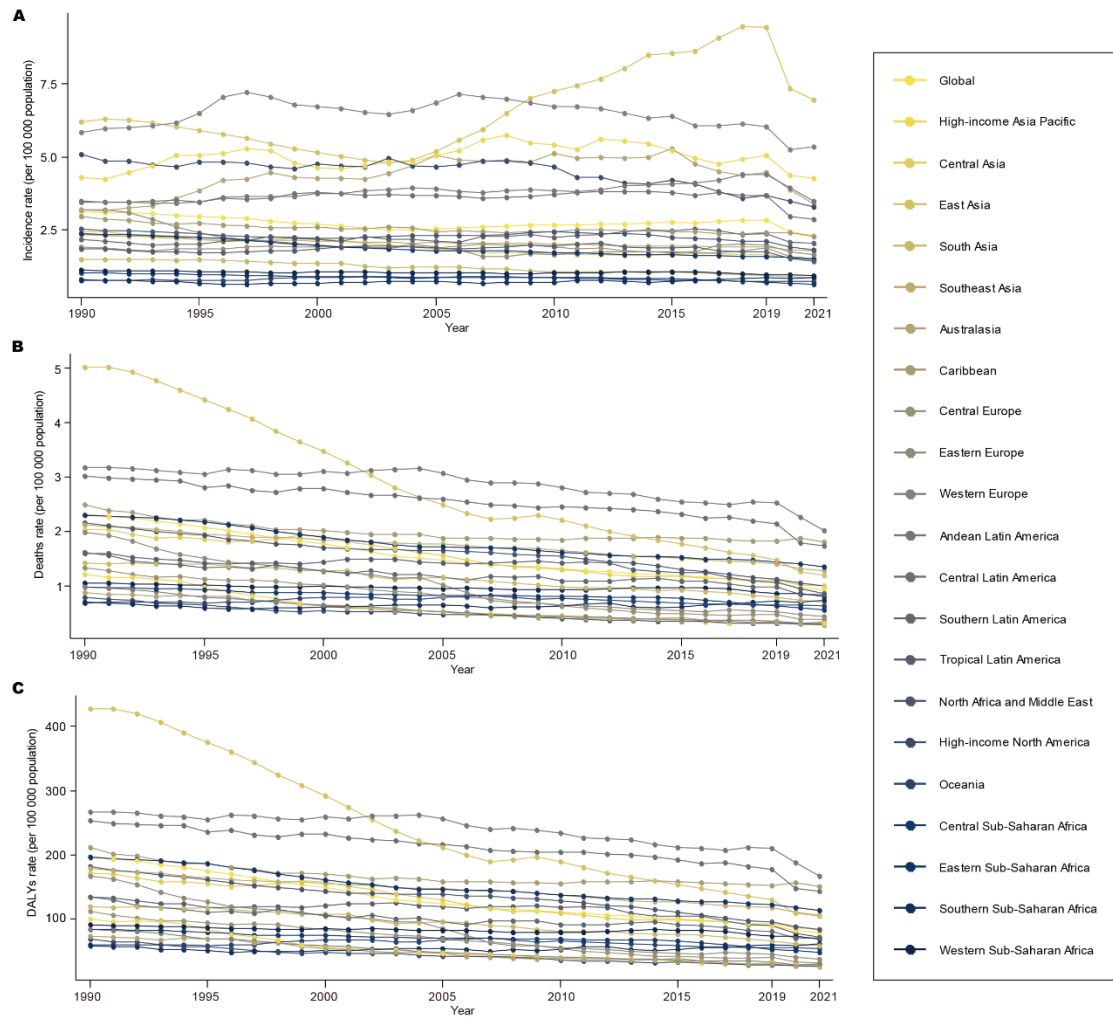
DALYs: disability-adjusted life year; SDI: socio-demographic index.

Figure S2: Incidence, deaths, and DALYs rates trends of childhood ALL in different age groups across SDI regions (1990-2021), related to Figure 2



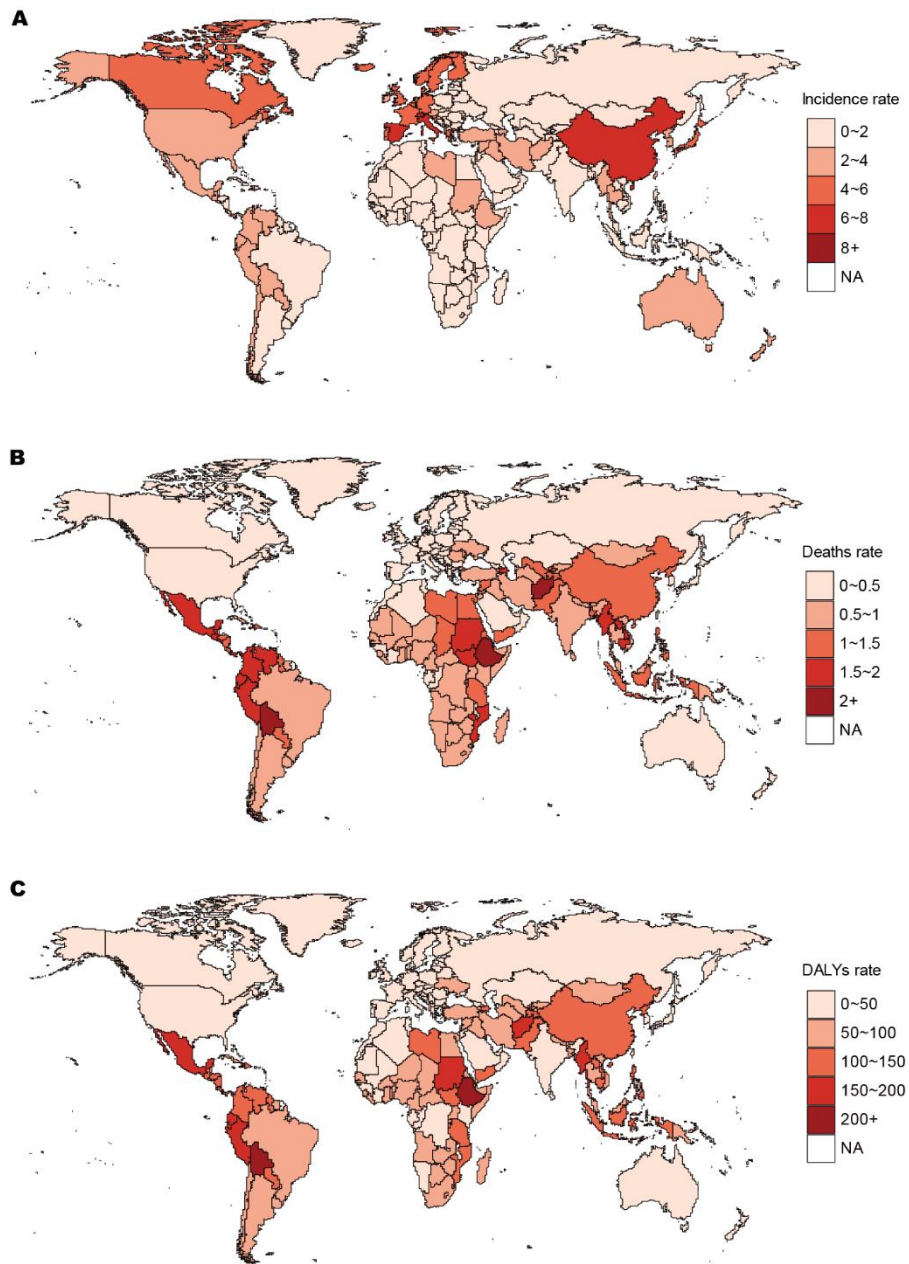
DALYs: disability-adjusted life year; SDI: socio-demographic index.

Figure S3: Trends in incidence, deaths, and DALYs rates of ALL in children across 21 GBD regions (1990-2021), related to Figure 3



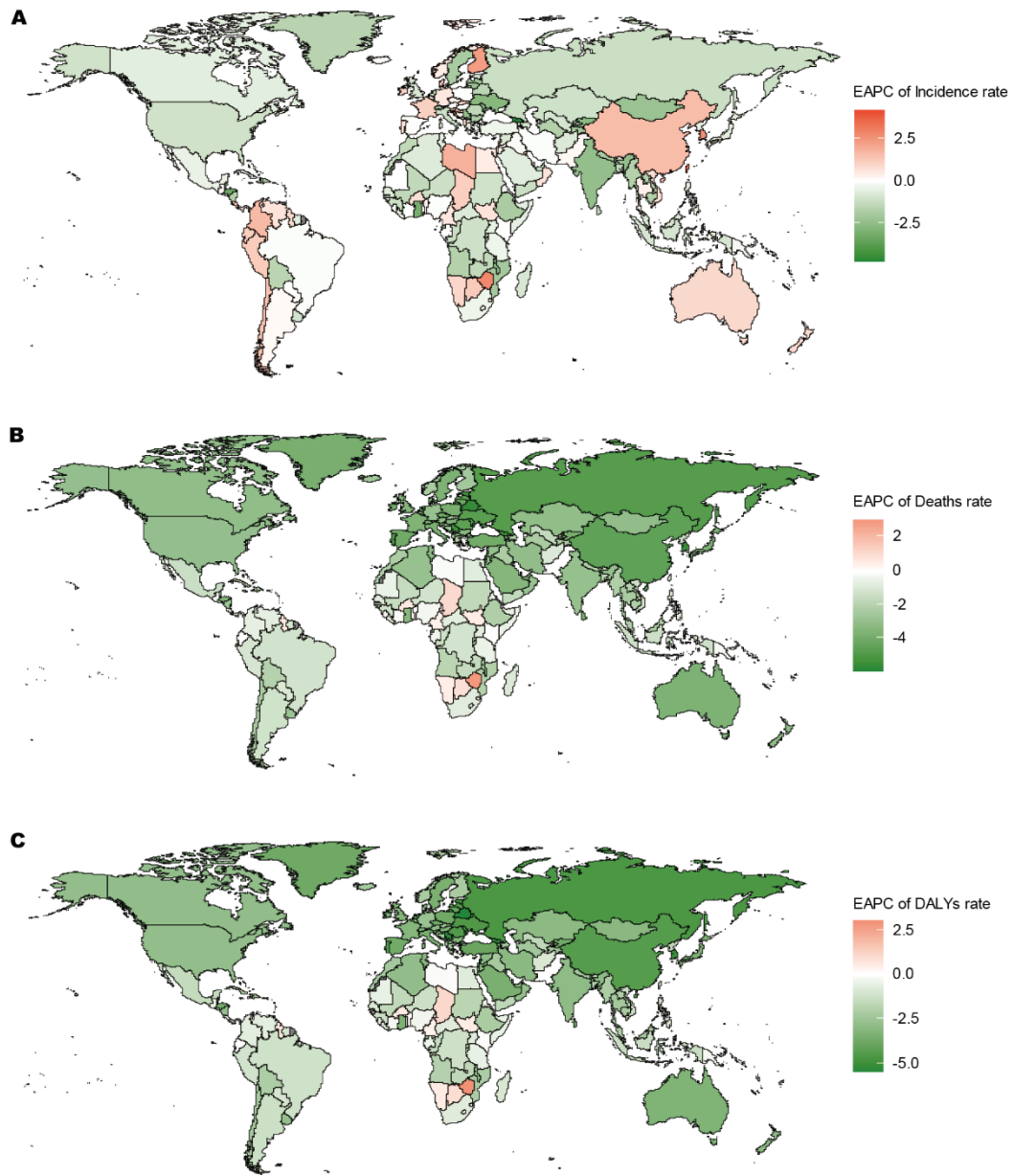
A: Trends in incidence rate.
 B: Trends in deaths rate.
 C: Trends in DALYs rate.
 DALYs: disability-adjusted life year.

Figure S4: Incidence, deaths, and DALYs rates of childhood ALL in 204 countries and territories in 2021, related to Figure 4



A: Trends in incidence rate.
B: Trends in deaths rate.
C: Trends in DALYs rate.
DALYs: disability-adjusted life year.

Figure S5: EAPC trends of childhood ALL in 204 countries and regions from 1990 to 2021, related to Figure 4



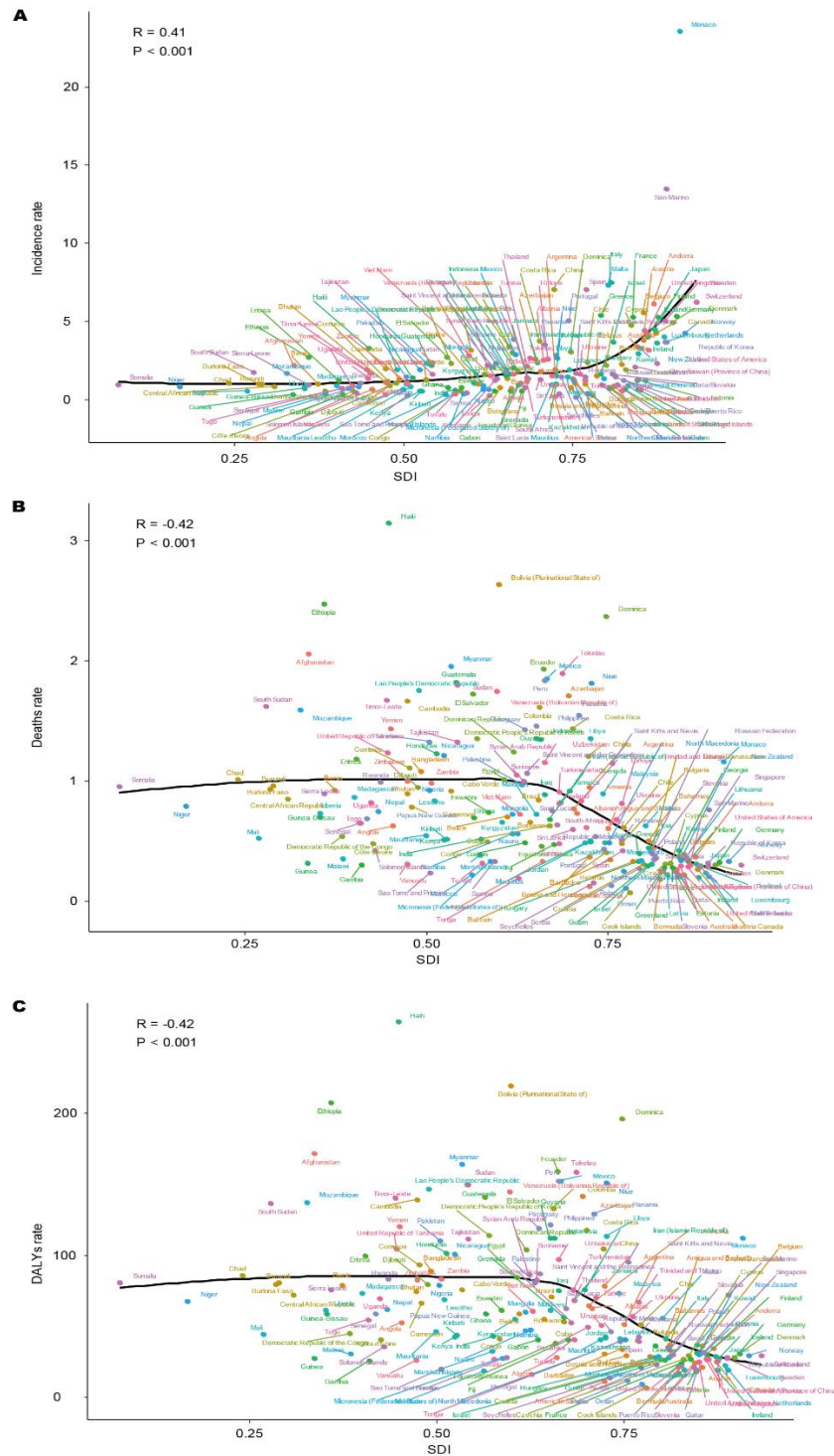
A: Trends in EAPC of incidence rate.

B: Trends in EAPC of deaths rate.

C: Trends in EAPC of DALYs rate.

DALYs: disability-adjusted life year; EAPC: estimated annual percentage changes.

Figure S6: Correlation between SDI and incidence, deaths, and DALYs rates of childhood ALL in 204 countries and territories in 2021, related to Figure 5



A: The correlation between SDI and incidence rate.
 B: The correlation between SDI and deaths rate.
 C: The correlation between SDI and DALYs rate.
 DALYs: disability-adjusted life year; SDI: socio-demographic index.

Table S1: Trends in DALYs at the global and SDI levels, 1990-2021, related to Figures 1 and 2 and Table 1

Characteristics	DALYs (95%UI)					
	1990		2021		1990-2021	
	Number	Rate(per100000)	Number	Rate(per100000)	Number change	EAPC (95%CI)
Global	3400708(2509935 to 4699438)	195.54(144.32 to 270.21)	1586755(1108074 to 1935867)	78.87(55.08 to 96.22)	-0.53(-0.68 to -0.33)	-2.79(-2.89 to -2.69)
Genders						
Male	1845615(990664 to 2832341)	206.56(110.88 to 317)	971579(603477 to 1263734)	93.59(58.13 to 121.73)	-0.47(-0.67 to -0.02)	-2.43(-2.53 to -2.33)
Female	1555093(1014465 to 2235038)	183.89(119.96 to 264.3)	615176(411164 to 749608)	63.18(42.23 to 76.99)	-0.6(-0.75 to -0.39)	-3.28(-3.38 to -3.17)
SDI quintiles						
High SDI	149614(141035 to 162247)	80.52(75.9 to 87.32)	50624(44673 to 56704)	29.34(25.89 to 32.87)	-0.66(-0.71 to -0.62)	-3.13(-3.25 to -3.01)
High-middle SDI	716514(533603 to 901662)	261.86(195.01 to 329.53)	161071(106202 to 208425)	69.76(46 to 90.27)	-0.78(-0.85 to -0.67)	-4.17(-4.32 to -4.03)
Middle SDI	1502663(1089235 to 2030500)	260.33(188.71 to 351.78)	505044(346718 to 625415)	89.09(61.16 to 110.33)	-0.66(-0.78 to -0.51)	-3.24(-3.38 to -3.1)
Low-middle SDI	668414(417413 to 1055787)	141.58(88.41 to 223.63)	442393(318467 to 541772)	76.3(54.92 to 93.43)	-0.34(-0.57 to 0.06)	-1.79(-1.9 to -1.69)
Low SDI	361298(180191 to 640206)	157.83(78.72 to 279.67)	426229(260952 to 563006)	92.61(56.7 to 122.33)	0.18(-0.31 to 1.38)	-1.66(-1.72 to -1.6)

DALYs: disability-adjusted life year; EAPC: estimated annual percentage changes; SDI: socio-demographic index; CI: confidence interval; UI: uncertainty interval.

Table S2: From 1990 to 2021, the incidence trends in 21 GBD regions, related to Figures 3 and 5

Regions	Incidence (95%UI)					
	1990		2021		1990-2021	
	Number	Rate (per100000)	Number	Rate (per100000)	Number change	EAPC (95%CI)
Andean Latin America	511(396 to 723)	3.44(2.67 to 4.87)	632(391 to 871)	3.49(2.16 to 4.81)	0.24(-0.36 to 0.98)	0.59(0.42 to 0.75)
Australasia	146(125 to 172)	3.19(2.72 to 3.75)	194(153 to 238)	3.38(2.67 to 4.15)	0.32(-0.01 to 0.73)	0.89(0.4 to 1.38)
Caribbean	338(237 to 500)	2.96(2.07 to 4.38)	260(178 to 388)	2.26(1.55 to 3.37)	-0.23(-0.43 to 0.01)	-0.59(-0.69 to -0.49)
Central Asia	604(509 to 713)	2.42(2.04 to 2.85)	412(334 to 534)	1.49(1.21 to 1.93)	-0.32(-0.47 to -0.12)	-1.48(-1.63 to -1.33)
Central Europe	559(505 to 624)	1.9(1.71 to 2.12)	269(221 to 330)	1.52(1.25 to 1.86)	-0.52(-0.62 to -0.38)	-0.34(-0.54 to -0.14)
Central Latin America	2228(2086 to 2407)	3.46(3.24 to 3.74)	1809(1492 to 2237)	2.85(2.35 to 3.52)	-0.19(-0.34 to 0.01)	-0.03(-0.27 to 0.22)
Central Sub-Saharan Africa	254(113 to 488)	1(0.45 to 1.93)	359(197 to 544)	0.61(0.34 to 0.93)	0.42(-0.17 to 2.3)	-1.18(-1.36 to -0.99)
East Asia	20439(14040 to 28574)	6.2(4.26 to 8.66)	18557(10025 to 27603)	6.94(3.75 to 10.32)	-0.09(-0.55 to 0.51)	1.56(0.98 to 2.14)
Eastern Europe	1639(1471 to 1825)	3.18(2.86 to 3.55)	579(514 to 654)	1.63(1.45 to 1.85)	-0.65(-0.7 to -0.59)	-1.66(-2.14 to -1.18)
Eastern Sub-Saharan Africa	2144(1080 to 3724)	2.37(1.19 to 4.11)	2648(1636 to 3839)	1.48(0.92 to 2.15)	0.23(-0.34 to 1.57)	-1.47(-1.57 to -1.37)

High-income Asia Pacific	1509(1293 to 1809)	4.29(3.67 to 5.14)	958(790 to 1130)	4.27(3.52 to 5.04)	-0.36(-0.51 to 0.19)	0.24(-0.08 to 0.55)
High-income North America	3126(2951 to 3330)	5.07(4.78 to 5.4)	2155(1945 to 2397)	3.28(2.96 to 3.65)	-0.31(-0.38 to 0.22)	-1(-1.24 to -0.76)
North Africa and Middle East	3543(2296 to 5310)	2.52(1.63 to 3.78)	3330(1949 to 4318)	1.82(1.06 to 2.36)	-0.06(-0.42 to 0.59)	-0.46(-0.66 to 0.25)
Oceania	20(10 to 37)	0.75(0.37 to 1.39)	36(18 to 67)	0.71(0.36 to 1.32)	0.79(0.26 to 1.54)	-0.15(-0.4 to 0.1)
South Asia	6373(3670 to 10311)	1.47(0.85 to 2.38)	4261(3028 to 5552)	0.84(0.6 to 1.09)	-0.33(-0.58 to 0.13)	-1.75(-1.86 to 1.64)
Southeast Asia	3958(2451 to 6337)	2.32(1.44 to 3.71)	3050(2117 to 3779)	1.77(1.23 to 2.19)	-0.23(-0.52 to 0.25)	-0.69(-0.74 to 0.63)
Southern Latin America	322(295 to 352)	2.16(1.97 to 2.36)	294(244 to 354)	2.03(1.68 to 2.44)	-0.09(-0.26 to 0.15)	0.44(0.23 to 0.65)
Southern Sub-Saharan Africa	162(115 to 230)	0.78(0.56 to 1.11)	207(146 to 264)	0.86(0.61 to 1.1)	0.28(-0.05 to 0.78)	0.49(0.22 to 0.76)
Tropical Latin America	979(864 to 1090)	1.83(1.61 to 2.03)	706(571 to 855)	1.41(1.14 to 1.7)	-0.28(-0.42 to 0.11)	-0.1(-0.38 to 0.18)
Western Europe	4152(3855 to 4492)	5.85(5.43 to 6.33)	3648(3294 to 4084)	5.36(4.84 to 6)	-0.12(-0.23 to 0.01)	-0.23(-0.51 to 0.06)
Western Sub-Saharan Africa	971(480 to 1524)	1.11(0.55 to 1.73)	1942(757 to 2825)	0.9(0.35 to 1.32)	1(0.15 to 2.39)	-0.34(-0.45 to 0.23)

EAPC: estimated annual percentage changes; CI: confidence interval; UI: uncertainty interval.

Table S3: From 1990 to 2021, the deaths trends in 21 GBD regions, related to Figures 3 and 5

Regions	Deaths (95%UI)					
	1990		2021		1990-2021	
	Number	Rate (per100000)	Number	Rate (per100000)	Number change	EAPC (95%CI)
Andean Latin America	472(364 to 678)	3.18(2.45 to 4.56)	366(240 to 486)	2.02(1.33 to 2.68)	-0.23(-0.57 to 0.17)	-1.06(-1.25 to -0.86)
Australasia	40(37 to 43)	0.88(0.81 to 0.95)	16(14 to 19)	0.28(0.24 to 0.33)	-0.6(-0.66 to -0.52)	-3.54(-3.73 to -3.35)
Caribbean	285(187 to 445)	2.5(1.64 to 3.9)	207(130 to 341)	1.8(1.13 to 2.96)	-0.27(-0.47 to 0.04)	-0.83(-0.98 to -0.68)
Central Asia	510(435 to 594)	2.04(1.74 to 2.38)	277(225 to 351)	1(0.81 to 1.27)	-0.46(-0.58 to -0.3)	-2.39(-2.57 to -2.2)
Central Europe	395(357 to 436)	1.34(1.21 to 1.48)	68(60 to 77)	0.39(0.34 to 0.43)	-0.83(-0.85 to -0.79)	-3.95(-4.16 to -3.74)
Central Latin America	1948(1826 to 2091)	3.03(2.84 to 3.25)	1100(935 to 1308)	1.73(1.47 to 2.06)	-0.44(-0.53 to -0.32)	-1.32(-1.5 to -1.13)
Central Sub-Saharan Africa	248(110 to 480)	0.98(0.43 to 1.9)	336(186 to 507)	0.57(0.32 to 0.86)	0.35(-0.21 to 2.23)	-1.31(-1.5 to -1.11)
East Asia	16535(11347 to 22888)	5.01(3.44 to 6.94)	3222(1905 to 4446)	1.21(0.71 to 1.66)	-0.81(-0.89 to -0.68)	-4.46(-4.64 to -4.28)
Eastern Europe	1021(935 to 1122)	1.98(1.82 to 2.18)	161(149 to 175)	0.45(0.42 to 0.49)	-0.84(-0.86 to -0.82)	-4.84(-5.13 to -4.56)
Eastern Sub-Saharan Africa	2089(1040 to 3639)	2.31(1.15 to 4.02)	2414(1510 to 3517)	1.35(0.85 to 1.97)	0.16(-0.38 to 1.43)	-1.67(-1.76 to -1.58)

High-income Asia Pacific	426(359 to 494)	1.21(1.02 to 1.4)	72(63 to 80)	0.32(0.28 to 0.35)	-0.83(-0.86 to -0.79)	-4.42(-4.7 to -4.14)
High-income North America	489(479 to 500)	0.79(0.78 to 0.81)	196(184 to 211)	0.3(0.28 to 0.32)	-0.6(-0.62 to -0.57)	-2.96(-3.07 to -2.84)
North Africa and Middle East	3048(1976 to 4584)	2.17(1.41 to 3.26)	1848(1041 to 2404)	1.01(0.57 to 1.31)	-0.39(-0.63 to -0.01)	-2.07(-2.24 to -1.89)
Oceania	19(9 to 34)	0.7(0.34 to 1.29)	32(17 to 60)	0.64(0.33 to 1.18)	0.73(0.18 to 1.5)	-0.23(-0.48 to 0.03)
South Asia	6167(3565 to 10085)	1.42(0.82 to 2.33)	3620(2624 to 4687)	0.71(0.52 to 0.92)	-0.41(-0.62 to -0.01)	-2.15(-2.29 to -2.01)
Southeast Asia	3635(2247 to 5883)	2.13(1.32 to 3.45)	2212(1512 to 2729)	1.28(0.88 to 1.58)	-0.39(-0.62 to -0.01)	-1.43(-1.51 to -1.34)
Southern Latin America	242(224 to 264)	1.62(1.5 to 1.77)	123(108 to 143)	0.85(0.74 to 0.99)	-0.49(-0.57 to -0.39)	-1.53(-1.71 to -1.35)
Southern Sub-Saharan Africa	146(105 to 206)	0.7(0.51 to 0.99)	178(126 to 227)	0.74(0.52 to 0.94)	0.22(-0.08 to 0.68)	0.27(0.05 to 0.48)
Tropical Latin America	858(755 to 957)	1.6(1.41 to 1.78)	438(359 to 518)	0.87(0.71 to 1.03)	-0.49(-0.58 to -0.39)	-1.19(-1.51 to -0.87)
Western Europe	699(677 to 719)	0.98(0.95 to 1.01)	227(210 to 244)	0.33(0.31 to 0.36)	-0.68(-0.7 to -0.65)	-3.55(-3.68 to -3.42)
Western Sub-Saharan Africa	935(464 to 1478)	1.06(0.53 to 1.68)	1758(701 to 2512)	0.82(0.33 to 1.17)	0.88(0.1 to 2.15)	-0.53(-0.64 to -0.42)

EAPC: estimated annual percentage changes; CI: confidence interval; UI: uncertainty interval.

Table S4: From 1990 to 2021, the DALYs trends in 21 GBD regions, related to Figures 3 and 5

Regions	DALYs (95%UI)					
	1990		2021		1990-2021	
	Number	Rate (per100000)	Number	Rate (per100000)	Number change	EAPC (95%CI)
Andean Latin America	39585(30404 to 57056)	266.53(204.71 to 384.17)	30317(19833 to 40288)	167.55(109.61 to 222.65)	-0.23(-0.58 to 0.17)	-1.09(-1.28 to -0.9)
Australasia	3391(3144 to 3669)	73.94(68.56 to 80.02)	1452(1246 to 1712)	25.34(21.74 to 29.88)	-0.57(-0.64 to -0.49)	-3.27(-3.46 to -3.08)
Caribbean	24101(15719 to 37827)	211.19(137.74 to 331.46)	17381(10859 to 28649)	151.07(94.38 to 249.01)	-0.28(-0.48 to -0.05)	-0.85(-1 to -0.69)
Central Asia	42881(36501 to 50035)	171.59(146.06 to 200.21)	23143(18736 to 29467)	83.62(67.7 to 106.47)	-0.46(-0.58 to -0.3)	-2.37(-2.54 to -2.2)
Central Europe	32851(29689 to 36379)	111.42(100.7 to 123.39)	5750(5054 to 6486)	32.48(28.55 to 36.64)	-0.82(-0.85 to -0.79)	-3.89(-4.09 to -3.7)
Central Latin America	162906(152397 to 175209)	253.03(236.71 to 272.14)	90648(76767 to 108162)	142.79(120.92 to 170.37)	-0.44(-0.54 to -0.32)	-1.36(-1.55 to -1.17)
Central Sub-Saharan Africa	21094(9171 to 40995)	83.38(36.25 to 162.05)	28023(15432 to 42677)	47.75(26.3 to 72.73)	0.33(-0.23 to 2.19)	-1.36(-1.56 to -1.16)
East Asia	1409668(964759 to 1956190)	427.39(292.5 to 593.08)	277916(162221 to 385772)	103.95(60.68 to 144.29)	-0.8(-0.89 to -0.68)	-4.38(-4.56 to -4.19)
Eastern Europe	85680(78415 to 94164)	166.49(152.37 to 182.98)	13624(12582 to 14913)	38.44(35.5 to 42.08)	-0.84(-0.86 to -0.82)	-4.76(-5.04 to -4.48)
Eastern Sub-Saharan Africa	178194(88537 to 311052)	196.75(97.75 to 343.44)	203405(126187 to 297789)	114(70.72 to 166.89)	0.14(-0.39 to 1.42)	-1.7(-1.79 to -1.62)

High-income Asia Pacific	35489(29968 to 40955)	100.82(85.14 to 116.35)	6457(5586 to 7227)	28.79(24.91 to 32.23)	-0.82(-0.85 to -0.77)	-4.11(-4.38 to -3.85)
High-income North America	42204(41234 to 43342)	68.43(66.85 to 70.27)	17485(16225 to 18894)	26.65(24.73 to 28.79)	-0.59(-0.61 to -0.55)	-2.82(-2.94 to -2.71)
North Africa and Middle East	256141(165494 to 387633)	182.33(117.8 to 275.92)	154064(86625 to 200537)	84.04(47.25 to 109.39)	-0.4(-0.63 to -0.01)	-2.07(-2.25 to -1.89)
Oceania	1590(776 to 2936)	59.34(28.94 to 109.54)	2750(1421 to 5087)	54.13(27.97 to 100.12)	0.73(0.19 to 1.5)	-0.22(-0.48 to 0.04)
South Asia	516282(297461 to 846735)	119.13(68.64 to 195.39)	298964(216649 to 388634)	58.96(42.73 to 76.65)	-0.42(-0.63 to -0.01)	-2.19(-2.32 to -2.05)
Southeast Asia	304595(186006 to 494432)	178.39(108.94 to 289.57)	184265(125855 to 227514)	106.73(72.89 to 131.78)	-0.4(-0.62 to -0.01)	-1.44(-1.52 to -1.36)
Southern Latin America	20120(18578 to 21905)	134.79(124.46 to 146.75)	10193(8912 to 11865)	70.32(61.48 to 81.85)	-0.49(-0.57 to -0.4)	-1.53(-1.71 to -1.35)
Southern Sub-Saharan Africa	12185(8674 to 17331)	58.89(41.92 to 83.77)	14691(10354 to 18766)	61.04(43.02 to 77.98)	0.21(-0.1 to 0.67)	0.27(0.05 to 0.49)
Tropical Latin America	71852(63160 to 80317)	134.02(117.8 to 149.81)	36396(29706 to 43132)	72.51(59.18 to 85.93)	-0.49(-0.59 to -0.39)	-1.22(-1.54 to -0.89)
Western Europe	59982(57898 to 61997)	84.46(81.53 to 87.3)	20950(19386 to 22940)	30.76(28.46 to 33.68)	-0.65(-0.68 to -0.62)	-3.27(-3.39 to -3.15)
Western Sub-Saharan Africa	79916(39174 to 126937)	90.94(44.58 to 144.44)	148882(58497 to 213080)	69.32(27.24 to 99.22)	0.86(0.08 to 2.13)	-0.55(-0.66 to -0.44)

DALYs: disability-adjusted life year; EAPC: estimated annual percentage changes; CI: confidence interval; UI: uncertainty interval.