

THE LANCET

Public Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
We post it as supplied by the authors.

Supplement to: Ju C, Wei L, Man KKC, et al. Global, regional, and national trends
in opioid analgesic consumption from 2015 to 2019: a longitudinal study.
Lancet Public Health 2022; **7**: e335–46.

Global, regional, and national trends in opioid analgesic consumption from 2015 to 2019: a longitudinal study

Supplementary appendix

Table of Contents

Methods S1: Additional data sources	3
Table S1. List of participating countries/regions in the IQVIA-MIDAS dataset and sector coverage.	4
Table S2. List of opioid analgesics and MME conversion factor	6
Table S3. List of opioid analgesics products with imputed formulation.	7
Table S4. Sensitivity analysis: worldwide, regional, and national levels of strong opioid analgesic consumption in 2015 and 2019 and average annual percentage change in consumption.	9
Table S5. Sensitivity analysis: worldwide, regional, and national levels of opioid analgesic consumption (including buprenorphine/methadone/levomethadone) in 2015 and 2019 and average annual percentage change in consumption.	11
Table S6. Sensitivity analysis: worldwide, regional, and national levels of opioid analgesic consumption in selected countries in 2015 and 2019 and average annual percentage change in consumption.	13
Table S7. Coefficient estimates in the multivariable analyses.	15
Table S8. Sensitivity analysis: national levels of opioid analgesic consumption in 2015-2016 and 2018-2019 and absolute change in consumption.	16
Figure S1. Average annual percentage change in worldwide opioid analgesic consumption from 2015 to 2019.	18
Figure S2. Scatter plots of opioid analgesic consumption and Gross Domestic Product (GDP) per capita in US\$, group by geographical location.	19
Figure S3. Scatter plot of opioid analgesic consumption and cancer (except leukaemia) prevalence group by geographical location.	20
Figure S4. Scatter plot of opioid analgesic consumption and leukaemia death group by geographical location.	21
Figure S5. Scatter plot of opioid analgesic consumption and Human Development Index (HDI) by cancer prevalence.	22

Figure S6. Sensitivity analysis: quarterly trends in strong opioid analgesic consumption at the regional level between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID.23

Figure S7. Sensitivity analysis: quarterly trends in opioid analgesic (including N02A buprenorphine, methadone, and levomethadone) consumption at the regional level between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID.....24

Figure S8. Sensitivity analysis: quarterly trends in opioid analgesic consumption at the regional level (only included countries with sales data available from both hospital and retail sectors) between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID...25

References:.....26

Methods S1: Additional data sources

Additional yearly country/region-level variables were obtained from other data sources: the mid-year population estimates of each country/region from the United Nations (UN) Population Division;¹ Human Development Index (HDI) data from the UN Development Programme;² and country/region income, measured by Gross Domestic Product (GDP) per capita in US dollar, from the World Bank.³ Cancer epidemiology (cancer (except leukaemia) death rate, leukaemia death rate, and cancer (except leukaemia) prevalence)⁴ of individual countries/regions were obtained from the Global Burden of Disease (GBD) data via the Global Health Data Exchange (GHDx).⁵ For the two aggregated regions (Central America and French West Africa), we calculated the median values across the member countries for use in the analyses.

Table S1. List of participating countries/regions in the IQVIA-MIDAS dataset and sector coverage.

Country	Sectors covered*	Percentage of market coverage†
Argentina	Retail	73%
Australia	Retail and hospital	90%
Austria	Retail and hospital	100%
Belarus	Retail and hospital	100%
Belgium	Retail and hospital	100%
Bosnia and Herzegovina	Retail and hospital	95%
Brazil	Retail and others	97%
Bulgaria	Retail and hospital	100%
Canada	Retail and hospital	100%
Central America‡	Retail	77%
Chile	Retail	71%
Colombia	Retail	79%
Croatia	Retail and hospital	100%
Czechia	Retail and hospital	95%
Denmark	Retail and hospital	100%
Ecuador	Retail	80%
Egypt	Retail	75%
Estonia	Retail	88%
Finland	Retail and hospital	100%
France	Retail and hospital	100%
French West Africa§	Retail	86%
Germany	Retail and hospital	100%
Greece	Retail	60%
Hungary	Retail and hospital	100%
India	Retail, hospital, and dispensing doctor	95%
Ireland	Retail and hospital	100%
Italy	Retail, hospital, and Local Health Unit	100%
Japan	Retail and hospital	100%
Kazakhstan	Retail and hospital	100%
Latvia	Retail and hospital	100%
Lebanon	Retail	77%
Lithuania	Retail and hospital	100%
Luxembourg	Retail	98%
Mainland China	Retail and hospital	72%
Mexico	Retail and others	100%
Morocco	Retail	88%
Netherlands	Retail and hospital	95%
New Zealand	Retail and hospital	100%
Norway	Retail and hospital	100%
Pakistan	Retail	85%
Peru	Retail	67%
Philippines	Retail and hospital	100%
Poland	Retail and hospital	100%
Portugal	Retail and hospital	100%

Puerto Rico	Retail and hospital	NA
Republic of Korea	Retail and hospital	100%
Romania	Retail and hospital	100%
Russian Federation	Retail and hospital	97%
Saudi Arabia	Retail and hospital	95%
Serbia	Retail and hospital	100%
Slovakia	Retail and hospital	97%
Slovenia	Retail and hospital	97%
South Africa	Retail and hospital	100%
Spain	Retail and hospital	100%
Sweden	Retail and hospital	98%
Switzerland	Retail and hospital	100%
Taiwan	Retail and hospital	97%
Thailand	Retail and hospital	93%
Tunisia	Retail and hospital	100%
Turkey	Retail and hospital	100%
Ukraine	Retail and hospital	100%
United Arab Emirates	Retail	45%
United Kingdom	Retail and hospital	92%
United States	Retail and hospital	100%
Uruguay	Retail and Mutuales	71%
Venezuela (Bolivarian Republic of)	Retail	78%

*48 out of the 66 countries/regions (73%) captured data from both retail and hospital sectors.

†For countries/regions where the data contributed to the MIDAS database do not have 100% market coverage within the panel, projections were made by IQVIA to estimate the total sales volume of each sales panel based on knowledge of the market share of participating wholesalers and retail or hospital pharmacies.

‡Data was aggregated from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama.

§Data was aggregated from Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Gabon, Guinea, Mali, Nigeria, Republic of Congo, Senegal, Togo.

NA, not available.

Table S2. List of opioid analgesics and MME conversion factor

Opioid analgesic	MME conversion factor	Strong opioid analgesic
Bezitramide ⁶	60	Y
Codeine ⁷	0.15	
Dextromoramide ⁸	4	Y
Dextropropoxyphene ⁹	0.1	
Diamorphine ⁸	Oral formulation: 1 Injection: 3	Y
Dihydrocodeine ⁷	0.25	
Dipipanone ⁸	0.5	Y
Fentanyl ^{8,10}	Tablet: 130 Film: 180 Nasal spray: 160 Patch: 100	Y
Hydrocodone ⁷	1	Y
Hydromorphone ^{8,10,11}	5	Y
Ketobemidone ¹⁰	2	Y
Levorphanol ^{7,12}	11	Y
Meptazinol ⁸	0.03	
Morphine ^{7,10}	Oral formulation: 1 Injection: 2	Y
Nalbuphine ⁷	1	Y
Nicomorphine ¹⁰	1	Y
Oxycodone ^{7,10}	1.5	Y
Oxymorphone ^{7,13}	3	Y
Pentazocine ^{7,8}	0.37	Y
Pethidine ^{8,10}	Oral formulation: 0.1 Injection: 0.24	Y
Piritramide ^{11,14}	0.75	Y
Tapentadol ^{7,15}	0.4	Y
Tilidine ¹⁶	0.1	
Tramadol ^{7,10}	0.1	
Trimeperidine ¹⁷	0.5	Y

MME: milligram morphine equivalent per 1,000 inhabitant per day.

Table S3. List of opioid analgesics products with imputed formulation.

Country	Molecule	Imputed formulation*
Argentina	Dextropropoxyphene	37.5 mg/1ml ampoule injection
Argentina	Morphine	20 mg/1ml ampoule for injection
Australia	Hydromorphone	400 microgram/1ml infusion bag
Australia	Morphine	1 mg/ml infusion bag
Australia	Morphine	10 mg/ml infusion bag
Australia	Oxycodone	10 mg/1ml infusion bag
Australia	Pethidine	50 mg/ml infusion bag
Canada	Codeine	30 mg tablet
Canada	Codeine	30 mg capsule
Canada	Oxycodone	5 mg tablet
Mainland China	Codeine	30 mg tablet
Mainland China	Fentanyl	50 microgram/hr transdermal patch
Germany	Fentanyl	100 microgram injection solution
Germany	Morphine	30 mg capsule
India	Morphine	50 mg/5 ml oral liquid
Italy	Fentanyl	200 microgram buccal tablet
Italy	Morphine	20 mg/ml ampoule for injection
Japan	Fentanyl	50 microgram/hr transdermal patch
Kazakhstan	Trimeperidine	20mg/ml ampoule for injection
Pakistan	Codeine	30 mg tablet
Pakistan	Dextropropoxyphene	32.5 mg tablet
Pakistan	Nalbuphine	10 mg/ml ampoule for injection
Pakistan	Pentazocine	25 mg tablet
Portugal	Morphine	10 mg/dose oral liquid
Puerto Rico	Codeine	10 mg capsule
Puerto Rico	Morphine	2 mg/ml prefilled syringe
Russian Federation	Codeine	30 mg tablet
Russian Federation	Morphine	10 mg/ml ampoule for injection
Slovenia	Morphine	10 mg/ml ampoule for injection
South Africa	Codeine	25 mg/5ml syrup
South Africa	Morphine	10 mg/ml ampoule for injection
Spain	Morphine	10 mg/dose oral liquid
Sweden	Codeine	30 mg/ml ampoule for injection
Sweden	Codeine	30mg oral solution
Sweden	Morphine	10 mg/ml ampoule for injection
Sweden	Morphine	30mg/ml solution for injection
Switzerland	Oxycodone	40 mg tablet
Taiwan	Pethidine	50 mg/ml ampoule for injection
United Kingdom	Morphine	10 mg/ml oral liquid
United Kingdom	Morphine	10 mg/ml ampoule for injection
United Kingdom	Morphine	10 mg/dose oral liquid
Ukraine	Codeine	30 mg/ml ampoule for injection

Ukraine	Morphine	10 mg/ml ampoule for injection
United States of America	Codeine	30 mg capsule
United States of America	Hydromorphone	10 mg/ml prefilled syringe
United States of America	Hydromorphone	10 mg/ml solution for injection
United States of America	Morphine	2 mg/ml prefilled syringe
United States of America	Morphine	1 mg/ml vial for injection

*When the strength or formulation of an opioid product is missing for a particular country/region and year, we identified the opioid product that has the same molecule and was sold the most in that country/region and year. We then imputed the missing formulation by that of the most-sold opioid product. Overall, only 41 out of 866 (4.7%) distinctive opioid analgesic products had the formulation/strength missing and were imputed.

Table S4. Sensitivity analysis: worldwide, regional, and national levels of strong opioid analgesic consumption in 2015 and 2019 and average annual percentage change in consumption.

	MME/TID in 2015 (95% CI)*	MME/TID in 2019 (95% CI)*	Average annual percentage change (95% CI)	P-value
Worldwide	24.06 (13.77 to 42.03)	21.65 (12.15 to 38.56)	0.36 (-2.76 to 3.58)	0.82
Africa	1.44 (0.14 to 14.85)	0.88 (0.03 to 29.95)	-16.26 (-40.82 to 18.48)	0.30
Egypt	0.70	0.61	-4.29 (-8.09 to -0.33)	0.041
French West Africa‡	0.07	0.01	-61.69 (-96.82 to 362.15)	0.31
Morocco	0.95	1.19	7.92 (-3.96 to 21.27)	0.13
South Africa	10.51	11.74	3.00 (-0.25 to 6.36)	0.061
Tunisia	11.65	12.05	0.99 (-0.83 to 2.84)	0.18
America (Central and Caribbean)	6.49 (0.02 to 2176.99)	6.24 (0.03 to 1544.88)	-1.89 (-7.00 to 3.51)	0.45
Central America§	1.50	1.32	-6.69 (-20.08 to 8.95)	0.25
Mexico	1.03	1.28	6.72 (0.91 to 12.86)	0.034
Puerto Rico	176.61	143.84	-5.16 (-9.82 to -0.25)	0.044
America (North)	1366.22 (835.06 to 2235.45)	800.95 (273.39 to 2346.55)	-12.93 (-15.46 to -10.34)	<0.0001
Canada	1443.20	902.71	-11.59 (-13.60 to -9.54)	<0.0001
United States of America	1293.39	710.61	-14.26 (-20.23 to -7.86)	0.0065
America (South)	0.51 (0.07 to 3.92)	0.43 (0.04 to 4.70)	-3.76 (-12.07 to 5.33)	0.39
Argentina	3.88	3.84	-0.95 (-4.87 to 3.13)	0.51
Brazil	8.23	6.94	-1.75 (-12.21 to 9.97)	0.65
Chile	0.22	0.33	10.09 (1.41 to 19.51)	0.034
Colombia	0.73	0.41	-10.87 (-26.46 to 8.02)	0.15
Ecuador	0.13	0.34	27.63 (22.56 to 32.91)	<0.0001
Peru	0.01	0.00	-31.24 (-65.15 to 35.68)	0.18
Uruguay	16.06	21.99	7.50 (4.94 to 10.13)	0.0024
Venezuela (Bolivarian Republic of)	0.03	0.02	-18.32 (-50.41 to 34.53)	0.29
Asia	4.06 (1.07 to 15.39)	5.77 (1.88 to 17.66)	9.20 (1.76 to 17.19)	0.016
India	0.01	0.18	99.79 (24.37 to 220.95)	0.019
Japan	139.92	272.09	14.25 (-10.10 to 45.20)	0.18
Kazakhstan	4.99	5.40	-5.52 (-32.13 to 31.54)	0.62
Lebanon	3.65	7.04	20.34 (-1.18 to 46.54)	0.058
Mainland China	6.42	8.94	8.58 (7.25 to 9.93)	0.0002
Pakistan	4.42	3.02	-6.49 (-19.09 to 8.06)	0.078
Philippines	0.97	1.23	5.01 (-2.34 to 12.90)	0.12
Republic of Korea	4.33	11.30	25.74 (20.84 to 30.85)	0.0004
Saudi Arabia	4.65	1.24	-24.32 (-54.68 to 26.39)	0.18
Taiwan	63.68	66.50	2.48 (-4.04 to 9.44)	0.32
Thailand	6.09	6.93	2.52 (-6.26 to 12.12)	0.44
Turkey	25.37	24.19	-1.19 (-2.13 to -0.24)	0.028
United Arab Emirates	0.41	0.79	14.87 (2.81 to 28.36)	0.029
Europe (East)	26.28 (11.56 to 59.76)	33.87 (19.41 to 59.07)	7.04 (2.79 to 11.46)	0.0017
Belarus	21.93	26.59	3.60 (-6.93 to 15.32)	0.37
Bosnia and Herzegovina	26.61	30.37	3.90 (-0.20 to 8.18)	0.057

Bulgaria	48.82	47.98	-1.43 (-5.89 to 3.23)	0.40
Croatia	86.72	71.83	-4.50 (-6.82 to -2.13)	0.0094
Romania	46.15	59.63	6.54 (4.57 to 8.54)	0.0017
Russian Federation	5.76	13.88	30.49 (5.73 to 61.05)	0.028
Serbia	63.63	66.68	1.30 (-1.78 to 4.47)	0.28
Ukraine	5.44	11.26	20.78 (14.65 to 27.25)	0.0014
Europe (West and Central)	298.66 (207.39 to 430.14)	310.57 (223.39 to 431.82)	0.81 (-0.31 to 1.94)	0.15
Austria	775.75	746.67	-0.93 (-1.33 to -0.52)	0.0054
Belgium	705.01	692.28	-0.66 (-2.11 to 0.82)	0.25
Czechia	257.96	309.87	4.64 (4.19 to 5.08)	<0.0001
Denmark	972.02	836.37	-3.86 (-5.91 to -1.77)	0.010
Estonia	40.33	70.98	10.98 (-4.05 to 28.37)	0.11
Finland	404.17	367.57	-2.14 (-3.33 to -0.94)	0.011
France	412.92	437.95	1.47 (0.66 to 2.29)	0.010
Germany	826.61	791.93	-1.16 (-1.71 to -0.61)	0.0068
Greece	82.27	100.53	6.55 (1.38 to 11.99)	0.027
Hungary	198.46	203.04	0.44 (-1.01 to 1.91)	0.41
Ireland	324.82	314.72	-1.24 (-3.02 to 0.56)	0.12
Italy	229.44	252.64	2.63 (0.19 to 5.14)	0.042
Latvia	75.53	98.25	7.46 (1.86 to 13.37)	0.023
Lithuania	80.43	80.49	-0.06 (-0.76 to 0.65)	0.81
Luxembourg	339.01	181.42	-14.64 (-16.35 to -12.91)	0.0001
Netherlands	614.38	703.39	3.76 (-1.09 to 8.85)	0.091
Norway	638.12	687.08	1.60 (0.20 to 3.02)	0.036
Poland	103.80	128.20	5.03 (0.45 to 9.82)	0.039
Portugal	140.81	193.75	8.03 (6.68 to 9.40)	0.0003
Slovakia	166.05	172.99	0.83 (-1.16 to 2.86)	0.28
Slovenia	228.63	175.36	-6.65 (-7.96 to -5.31)	0.0006
Spain	594.06	695.25	3.86 (1.89 to 5.86)	0.0080
Sweden	596.28	541.15	-2.46 (-3.23 to -1.69)	0.0021
Switzerland	740.98	846.36	3.27 (1.60 to 4.97)	0.0082
United Kingdom	694.44	615.73	-3.09 (-5.29 to -0.84)	0.023
Oceania	542.40 (13.80 to 21324.25)	422.29 (30.70 to 5808.63)	-6.02 (-8.84 to -3.11)	0.0019
Australia	816.18	565.36	-8.69 (-11.93 to -5.34)	0.0040
New Zealand	360.44	315.43	-3.27 (-6.18 to -0.27)	0.041

*Worldwide and regional estimates with 95%CI were calculated by pooling the estimates from individual countries using a random-effects model.

CI: confidence interval; MME/TID: milligram morphine equivalent per 1,000 inhabitant per day.

‡Data was aggregated from Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Gabon, Guinea, Mali, Nigeria, Republic of Congo, Senegal, Togo.

§Data was aggregated from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama.

Table S5. Sensitivity analysis: worldwide, regional, and national levels of opioid analgesic consumption (including buprenorphine/methadone/levomethadone) in 2015 and 2019 and average annual percentage change in consumption.

	MME/TID in 2015 (95% CI)*	MME/TID in 2019 (95% CI)*	Average annual percentage change (95% CI)	P-value
Worldwide	32.25 (19.26 to 53.97)	35.95 (21.40 to 60.42)	4.44 (0.69 to 8.34)	0.020
Africa	1.66 (0.13 to 20.98)	1.01 (0.03 to 39.38)	-16.00 (-40.67 to 18.92)	0.31
Egypt	0.70	0.61	-4.29 (-8.09 to 0.33)	0.041
French West Africa‡	0.08	0.01	-61.54 (-96.80 to 362.30)	0.31
Morocco	0.95	1.45	12.41 (-4.10 to 31.77)	0.10
South Africa	21.33	18.77	-1.15 (-13.38 to 12.82)	0.80
Tunisia	11.65	12.70	2.20 (1.10 to 3.32)	0.0078
America (Central and Caribbean)	10.08 (0.02 to 6541.36)	12.29 (0.02 to 6081.46)	4.79 (0.02 to 9.79)	0.049
Central America§	1.51	2.13	5.56 (-12.26 to 27.01)	0.42
Mexico	1.69	2.07	7.58 (-2.02 to 18.13)	0.089
Puerto Rico	401.96	420.27	1.33 (-1.26 to 3.99)	0.20
America (North)	1660.88 (355.95 to 7748.85)	1075.56 (72.98 to 15852.78)	-10.74 (-14.26 to -7.06)	0.0003
Canada	1971.41	1451.13	-7.87 (-9.94 to -5.76)	0.0014
United States of America	1399.18	797.27	-13.51 (-20.20 to -6.26)	0.011
America (South)	0.66 (0.08 to 5.17)	1.75 (0.31 to 10.07)	27.14 (6.60 to 51.63)	0.0092
Argentina	5.18	5.54	1.04 (-2.84 to 5.09)	0.46
Brazil	10.54	9.43	-0.66 (-11.08 to 10.99)	0.86
Chile	0.38	0.69	14.95 (7.08 to 23.40)	0.0083
Colombia	1.14	0.82	-6.66 (-18.89 to 7.40)	0.22
Ecuador	0.15	4.24	137.22 (29.37 to 334.99)	0.020
Peru	0.02	1.27	193.85 (50.63 to 473.24)	0.014
Uruguay	18.74	29.74	11.34 (7.83 to 14.96)	0.0018
Venezuela (Bolivarian Republic of)	0.03	0.02	-18.32 (-50.41 to 34.53)	0.29
Asia	6.02 (2.38 to 15.28)	7.57 (2.92 to 19.63)	5.86 (0.66 to 11.32)	0.027
India	1.39	3.46	24.46 (2.06 to 51.77)	0.039
Japan	142.18	275.20	14.17 (-9.86 to 44.61)	0.17
Kazakhstan	5.00	5.40	-5.54 (-32.15 to 31.51)	0.62
Lebanon	3.65	7.04	20.34 (-1.18 to 46.54)	0.058
Mainland China	6.59	9.04	8.13 (7.39 to 8.87)	<0.0001
Pakistan	5.03	3.81	-4.62 (-16.18 to 8.53)	0.33
Philippines	0.97	1.23	5.01 (-2.33 to 12.90)	0.12
Republic of Korea	4.72	13.96	30.28 (26.39 to 34.29)	0.0001
Saudi Arabia	4.65	1.24	-24.31 (-54.68 to 26.41)	0.18
Taiwan	64.22	66.85	2.40 (-4.06 to 9.30)	0.33
Thailand	7.99	7.93	4.48 (-15.63 to 29.38)	0.56
Turkey	25.37	24.19	-1.19 (-2.13 to -0.24)	0.028
United Arab Emirates	0.41	0.79	14.95 (2.86 to 28.46)	0.028
Europe (East)	36.25 (13.73 to 95.71)	57.70 (29.27 to 113.77)	12.61 (4.71 to 21.12)	0.0023
Belarus	25.24	29.19	4.21 (-5.24 to 14.60)	0.26
Bosnia and Herzegovina	45.31	52.79	4.37 (0.57 to 8.31)	0.035
Bulgaria	48.86	48.06	-1.42 (-5.88 to 3.26)	0.40
Croatia	276.41	303.98	2.64 (1.39 to 3.91)	0.0066
Romania	51.83	64.38	5.45 (2.86 to 8.10)	0.0065
Russian Federation	6.77	14.99	27.56 (4.94 to 55.05)	0.029
Serbia	80.97	86.29	1.82 (-0.56 to 4.26)	0.093
Ukraine	6.80	65.59	71.76 (11.77 to 163.68)	0.028

Europe (West and Central)	384.44 (278.19 to 531.29)	400.09 (292.63 to 547.03)	1.09 (-0.16 to 2.36)	0.088
Austria	780.08	752.56	-0.87 (-1.29 to -0.46)	0.0068
Belgium	707.00	707.57	-0.21 (-1.37 to 0.97)	0.61
Czechia	309.72	377.09	5.13 (3.80 to 6.49)	0.0011
Denmark	1394.51	1188.53	-4.20 (-5.79 to -2.57)	0.0039
Estonia	175.11	115.65	-6.32 (-36.25 to 37.66)	0.63
Finland	410.89	376.28	-1.95 (-3.18 to -0.70)	0.016
France	413.77	438.58	1.46 (0.64 to 2.27)	0.011
Germany	890.09	888.79	-0.15 (-0.67 to 0.38)	0.44
Greece	106.66	125.68	5.14 (1.59 to 8.81)	0.019
Hungary	207.95	206.67	-0.13 (-0.55 to 0.30)	0.42
Ireland	741.24	723.20	-0.94 (-2.58 to 0.73)	0.17
Italy	436.97	514.75	4.26 (0.67 to 7.98)	0.032
Latvia	75.71	98.25	7.40 (1.78 to 13.33)	0.024
Lithuania	108.56	120.20	2.91 (-0.08 to 5.98)	0.053
Luxembourg	497.01	361.26	-7.88 (-8.74 to -7.01)	0.0001
Netherlands	725.19	846.76	4.07 (-0.49 to 8.83)	0.066
Norway	669.56	744.14	2.47 (1.09 to 3.86)	0.011
Poland	118.90	148.25	5.43 (1.60 to 9.41)	0.020
Portugal	219.24	361.16	12.42 (8.42 to 16.57)	0.0020
Slovakia	204.42	216.19	0.95 (-1.51 to 3.47)	0.31
Slovenia	288.04	238.28	-4.99 (-7.13 to -2.81)	0.0056
Spain	717.38	910.70	5.91 (3.53 to 8.34)	0.0040
Sweden	640.14	596.33	-1.81 (-2.71 to -0.89)	0.0082
Switzerland	895.61	1035.26	3.56 (1.33 to 5.83)	0.014
United Kingdom	735.57	694.36	-1.84 (-3.37 to -0.30)	0.032
Oceania	760.21 (23.49 to 24609.8)	678.51 (23.22 to 19828.98)	-2.76 (-3.79 to -1.71)	0.0005
Australia	1119.53	987.83	-3.00 (-4.81 to -1.17)	0.014
New Zealand	516.27	466.02	-2.51 (-4.82 to -0.13)	0.044

*Worldwide and regional estimates with 95%CI were calculated by pooling the estimates from individual countries using a random-effects model.

CI: confidence interval; MME/TID: milligram morphine equivalent per 1,000 inhabitant per day.

‡Data was aggregated from Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Gabon, Guinea, Mali, Nigeria, Republic of Congo, Senegal, Togo.

§Data was aggregated from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama.

Table S6. Sensitivity analysis: worldwide, regional, and national levels of opioid analgesic consumption in selected countries in 2015 and 2019 and average annual percentage change in consumption.

	MME/TID in 2015 (95%CI)*	MME/TID in 2019 (95%CI)*	Average annual percentage change (95%CI)	P-value
Worldwide	43.21 (27.22 to 68.60)	42.48 (26.92 to 67.06)	2.37 (0.79 to 3.97)	0.0033
Africa	14.75 (1.77 to 123.03)	13.58 (7.45 to 24.76)	-0.82 (-6.74 to 5.47)	0.76
South Africa	18.68	14.52	-3.76 (-18.03 to 13.00)	0.50
Tunisia	11.65	12.70	2.20 (1.10 to 3.32)	0.0078
America (Central and Caribbean)	-	-	-	-
Mexico	1.20	1.48	6.38 (1.67 to 11.30)	0.023
America (North)	1450.99 (672.57 to 3130.66)	853.46 (229.89 to 3168.46)	-12.84 (-15.34 to -10.27)	<0.0001
Canada	1580.67	987.60	-11.61 (-13.78 to -9.39)	<0.0001
United States of America	1331.99	737.51	-14.06 (-20.03 to -7.63)	0.0068
America (South)	-	-	-	-
Brazil	8.23	6.94	-1.75 (-12.21 to 9.97)	0.65
Asia	8.18 (2.81 to 23.83)	10.09 (3.19 to 31.89)	4.58 (-1.56 to 11.12)	0.14
India	1.39	3.45	24.45 (2.05 to 51.78)	0.039
Japan	142.05	274.87	14.16 (-9.91 to 44.65)	0.17
Kazakhstan	5.00	5.40	-5.54 (-32.15 to 31.51)	0.62
Mainland China	6.48	8.99	8.49 (7.18 to 9.81)	<0.0001
Philippines	0.97	1.23	5.01 (-2.34 to 12.90)	0.12
Republic of Korea	4.72	13.96	30.28 (26.39 to 34.29)	0.0001
Saudi Arabia	4.65	1.24	-24.32 (-54.68 to 26.39)	0.18
Taiwan	63.68	66.50	2.48 (-4.04 to 9.44)	0.32
Thailand	6.10	6.94	2.52 (-6.24 to 12.09)	0.44
Turkey	25.37	24.19	-1.19 (-2.13 to -0.24)	0.028
Europe (East)	28.90 (12.95 to 64.47)	38.14 (20.91 to 69.57)	7.68 (3.99 to 11.49)	0.0001
Belarus	21.93	26.59	3.60 (-6.93 to 15.32)	0.37
Bosnia and Herzegovina	43.08	47.93	2.87 (-0.04 to 5.86)	0.052
Bulgaria	48.82	47.98	-1.43 (-5.89 to 3.23)	0.40
Croatia	86.72	104.10	5.41 (2.46 to 8.45)	0.010
Romania	49.50	62.05	5.71 (3.75 to 7.71)	0.0025
Russian Federation	6.77	14.99	27.53 (4.97 to 54.95)	0.029
Serbia	63.63	66.68	1.30 (-1.78 to 4.47)	0.28
Ukraine	5.71	11.35	19.51 (12.80 to 26.62)	0.0022
Europe (West and Central)	370.48 (264.81 to 518.32)	399.22 (290.41 to 548.73)	1.79 (0.88 to 2.71)	0.0002
Austria	776.54	747.98	-0.91 (-1.32 to -0.49)	0.0061
Belgium	705.01	705.69	-0.20 (-1.36 to 0.97)	0.62
Czechia	309.24	376.58	5.14 (3.80 to 6.50)	0.0011
Denmark	991.23	860.81	-3.62 (-5.72 to -1.48)	0.013
Finland	404.17	367.57	-2.14 (-3.33 to -0.94)	0.011
France	412.92	437.95	1.47 (0.66 to 2.29)	0.010
Germany	881.40	879.04	-0.17 (-0.67 to 0.33)	0.36
Hungary	198.46	203.04	0.44 (-1.01 to 1.91)	0.41
Ireland	372.26	417.14	2.47 (0.11 to 4.89)	0.045
Italy	286.58	344.29	4.87 (1.82 to 8.02)	0.014
Latvia	75.71	98.25	7.40 (1.78 to 13.33)	0.017
Lithuania	80.44	80.49	-0.06 (-0.76 to 0.64)	0.80
Netherlands	617.71	717.34	4.12 (-0.81 to 9.30)	0.077
Norway	651.33	719.37	2.29 (0.84 to 3.75)	0.015

Poland	105.01	131.43	5.46 (0.92 to 10.19)	0.031
Portugal	211.16	355.97	13.43 (10.73 to 16.19)	<0.0001
Slovakia	204.03	215.79	0.95 (-1.52 to 3.48)	0.31
Slovenia	248.11	204.50	-5.05 (-6.76 to -3.30)	0.0029
Spain	675.04	863.14	6.15 (3.74 to 8.61)	0.0037
Sweden	614.20	572.16	-1.83 (-2.70 to -0.94)	0.0073
Switzerland	773.84	897.60	3.68 (1.81 to 5.59)	0.0080
United Kingdom	706.81	638.72	-2.63 (-4.86 to -0.34)	0.035
Oceania	656.29 (52.30 to 8235.42)	580.85 (55.14 to 6118.67)	-2.96 (-4.20 to -1.70)	0.0009
Australia	869.71	754.88	-3.40 (-5.85 to -0.88)	0.024
New Zealand	495.25	446.94	-2.52 (-4.88 to -0.10)	0.045

*Worldwide and regional estimates with 95%CI were calculated by pooling the estimates from individual countries using a random-effects model.

CI: confidence interval; MME/TID: milligram morphine equivalent per 1,000 inhabitant per day

Table S7. Coefficient estimates in the multivariable analyses.

	Main analysis	Sensitivity analysis: covariates untransformed
Year*	-0.010 (95% CI, -0.050 to 0.029; <i>P</i> -value, 0.60)	-0.012 (95% CI, -0.053 to 0.028; <i>P</i> -value, 0.55)
Geographical location	<i>P</i> <0.0001	<i>P</i> <0.0001
Africa	-1.95 (95% CI, -4.66 to 0.75)	-2.62 (95% CI, -5.18 to -0.05)
America (Central and Caribbean)	-1.43 (95% CI, -3.69 to 0.83)	-1.74 (95% CI, -4.08 to 0.61)
America (North)	0.48 (95% CI, -1.74 to 2.71)	0.57 (95% CI, -1.78 to 2.92)
America (South)	-4.06 (95% CI, -6.02 to -2.09)	-4.20 (95% CI, -6.25 to -2.15)
Asia	-1.96 (95% CI, -3.99 to 0.07)	-2.45 (95% CI, -4.53 to -0.38)
Europe (East)	-1.84 (95% CI, -4.01 to 0.33)	-2.13 (95% CI, -4.36 to 0.10)
Europe (West and Central)	-0.72 (95% CI, -2.43 to 0.98)	-0.84 (95% CI, -2.64 to 0.95)
Oceania	Reference	Reference
Cancer (except leukaemia) prevalence	-0.12 (95% CI, -1.00 to 0.75; <i>P</i> -value, 0.78)	0.0003 (95% CI, -0.0072 to 0.0077; <i>P</i> -value, 0.94)
Cancer (except leukaemia) death rate	1.50 (95% CI, 0.41 to 2.58; <i>P</i> -value, 0.0072)	0.85 (95% CI, 0.15 to 1.56; <i>P</i> -value, 0.017)
Leukaemia death rate	0.35 (95% CI, -1.26 to 1.97; <i>P</i> -value, 0.67)	-1.21 (95% CI, -24.44 to 22.03; <i>P</i> -value, 0.92)
HDI	5.42 (95% CI, 0.26 to 10.59; <i>P</i> -value, 0.040)	10.37 (95% CI, 5.20 to 15.54; <i>P</i> -value, 0.0001)
GDP per capita	0.28 (95% CI, -0.06 to 0.62; <i>P</i> -value, 0.11)	1.14*10 ⁻⁶ (95% CI, -2.74*10 ⁻⁶ to 5.01*10 ⁻⁶ ; <i>P</i> -value, 0.57)

Abbreviations: GDP, Gross Domestic Product; HDI, Human Development Index; CI, confidence interval.

*Average annual percentage change was calculated as [exp(the coefficient of the year variable)-1] *100%.

Table S8. Sensitivity analysis: national levels of opioid analgesic consumption in 2015-2016 and 2018-2019 and absolute change in consumption.

	MME/TID in 2015-2016	MME/TID in 2018-2019	Absolute change
Africa			
Egypt	0.72	0.62	-0.10
French West Africa‡	0.07	0.01	-0.06
Morocco	0.87	1.27	0.40
South Africa	15.60	14.33	-1.27
Tunisia	11.83	12.64	0.81
America (Central and Caribbean)			
Central America§	1.52	1.69	0.17
Mexico	1.22	1.49	0.27
Puerto Rico	188.72	161.05	-27.67
America (North)			0.00
Canada	1528.26	1044.14	-484.12
United States of America	1306.73	828.27	-478.46
America (South)			
Argentina	3.88	3.72	-0.16
Brazil	7.35	7.28	-0.07
Chile	0.39	0.58	0.19
Colombia	0.78	0.76	-0.02
Ecuador	0.32	3.89	3.57
Peru	0.06	1.01	0.95
Uruguay	18.84	25.16	6.32
Venezuela (Bolivarian Republic of)	0.05	0.03	-0.02
Asia			
India	1.43	2.78	1.35
Japan	143.03	209.72	66.69
Kazakhstan	5.33	4.07	-1.26
Lebanon	3.76	6.82	3.06
Mainland China	6.75	8.62	1.87
Pakistan	4.16	3.75	-0.41
Philippines	1.04	1.18	0.14
Republic of Korea	5.49	12.02	6.53
Saudi Arabia	2.96	1.17	-1.79
Taiwan	63.26	70.05	6.79
Thailand	5.95	6.34	0.39
Turkey	25.16	24.27	-0.89
United Arab Emirates	0.51	0.73	0.22
Europe (East)			
Belarus	21.61	23.61	2.00
Bosnia and Herzegovina	43.83	47.85	4.02
Bulgaria	49.94	46.88	-3.06
Croatia	86.43	102.68	16.25
Romania	50.25	59.30	9.05
Russian Federation	7.24	16.45	9.21
Serbia	62.41	65.03	2.62
Ukraine	5.99	10.39	4.40
Europe (West and Central)			
Austria	774.37	753.84	-20.53

Belgium	710.93	703.35	-7.58
Czechia	314.69	366.46	51.77
Denmark	995.61	888.79	-106.82
Estonia	52.41	65.96	13.55
Finland	400.26	376.73	-23.53
France	413.93	432.39	18.46
Germany	884.67	878.26	-6.41
Greece	105.77	125.14	19.37
Hungary	201.58	203.68	2.10
Ireland	385.98	411.71	25.73
Italy	297.63	344.26	46.63
Latvia	74.13	93.11	18.98
Lithuania	80.59	80.32	-0.27
Luxembourg	320.72	209.86	-110.86
Netherlands	645.09	732.06	86.97
Norway	664.90	708.40	43.50
Poland	112.69	131.07	18.38
Portugal	232.26	335.15	102.89
Slovakia	211.23	215.23	4.00
Slovenia	246.67	209.78	-36.89
Spain	710.83	846.22	135.39
Sweden	614.33	580.54	-33.79
Switzerland	800.73	890.23	89.50
United Kingdom	712.33	656.16	-56.17
Oceania			
Australia	864.71	781.31	-83.40
New Zealand	496.13	459.85	-36.28

MME/TID: milligram morphine equivalent per 1,000 inhabitant per day.

‡Data was aggregated from Benin, Burkina Faso, Cameroon, Chad, Côte d'Ivoire, Gabon, Guinea, Mali, Nigeria, Republic of Congo, Senegal, Togo.

§Data was aggregated from Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama.

Average annual percentage change in opioid consumption between 2015 and 2019

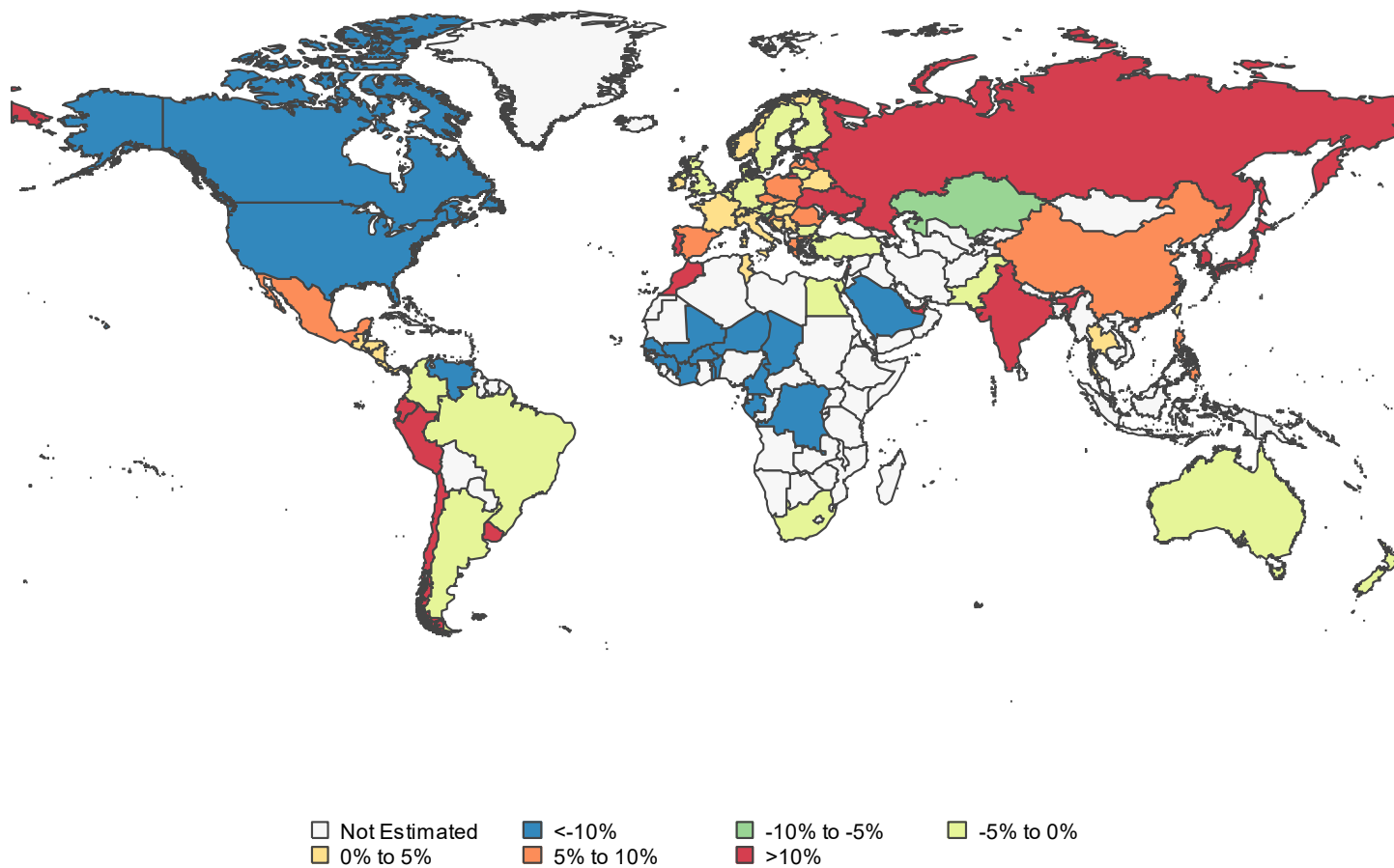


Figure S1. Average annual percentage change in worldwide opioid analgesic consumption from 2015 to 2019.

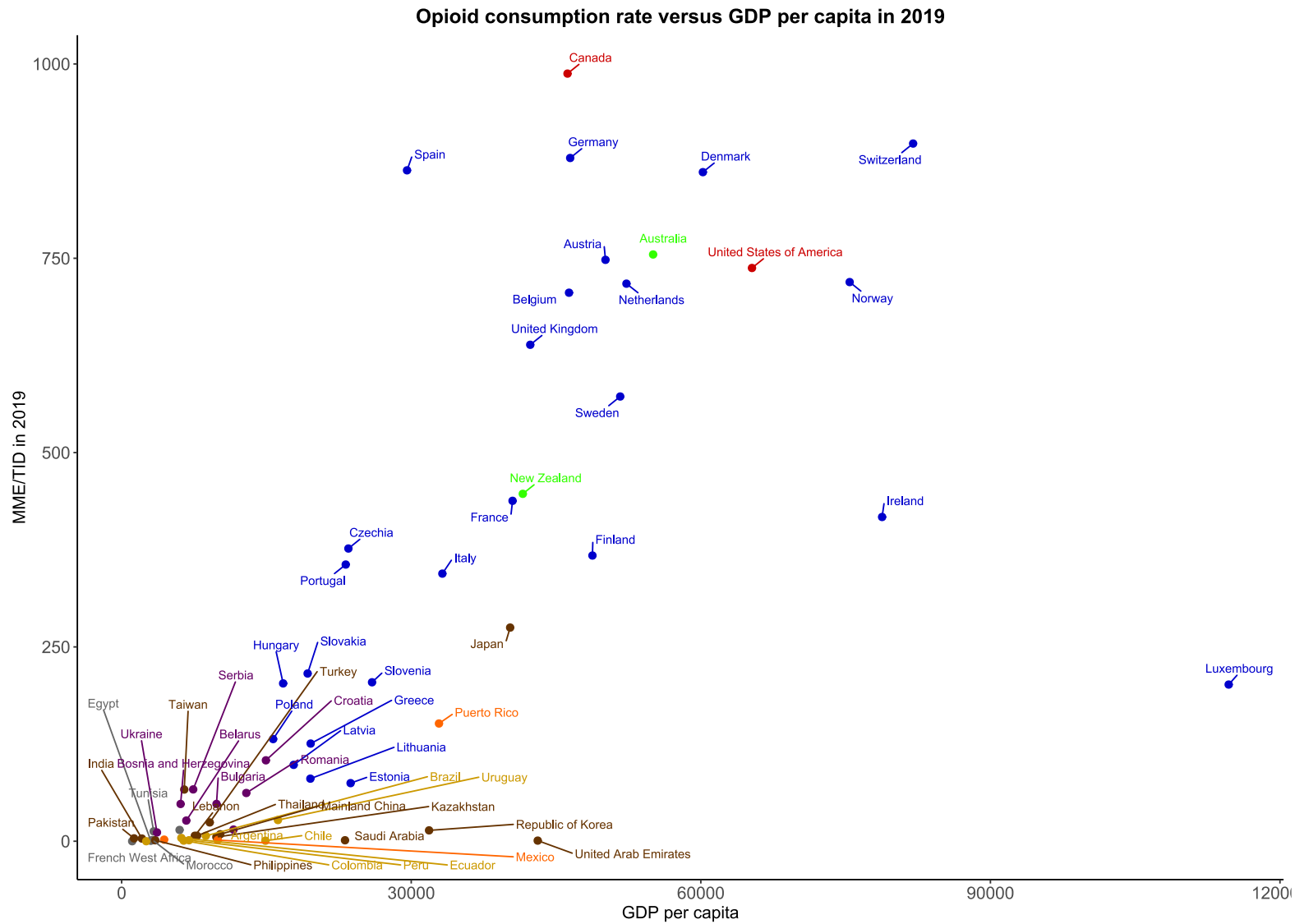


Figure S2. Scatter plots of opioid analgesic consumption and Gross Domestic Product (GDP) per capita in US\$, group by geographical location.

(Grey marker, Africa; orange marker, America (Central and Caribbean); red marker, America (North); yellow marker, America (South); brown marker, Asia; purple marker, Europe (East); blue marker, Europe (West and Central); green marker, Oceania)

(C) Opioid consumption rate versus cancer (except leukaemia) prevalence in 2019

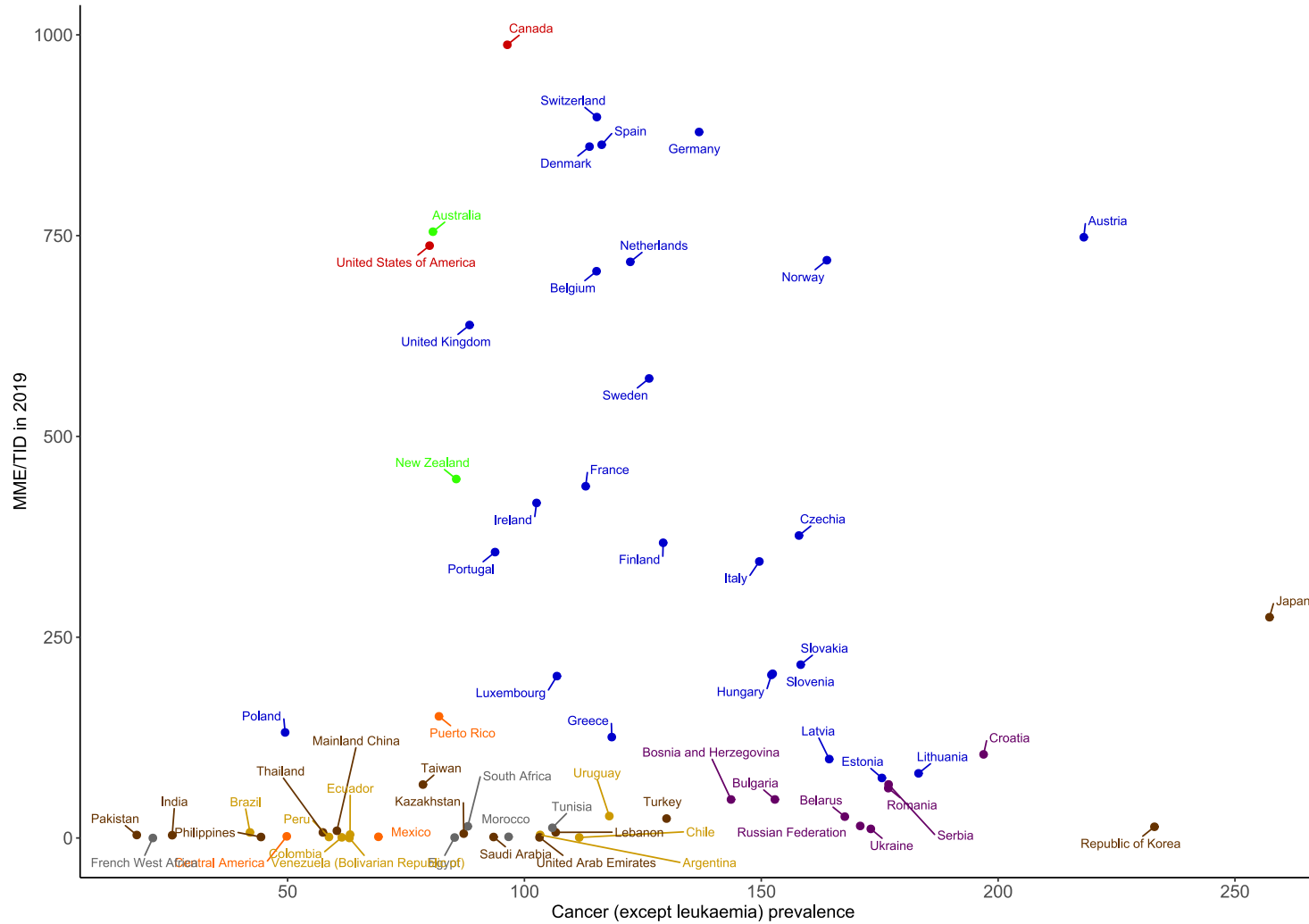


Figure S3. Scatter plot of opioid analgesic consumption and cancer (except leukaemia) prevalence group by geographical location.

(Cancer prevalence rates were measured in number of cancer deaths per 1,000 population. Data points were grouped by geographical location of each country/region: grey marker, Africa; orange marker, America (Central and Caribbean); red marker, America (North); yellow marker, America (South); brown marker, Asia; purple marker, Europe (East); blue marker, Europe (West and Central); green marker, Oceania)

Opioid consumption rate versus HDI in 2019

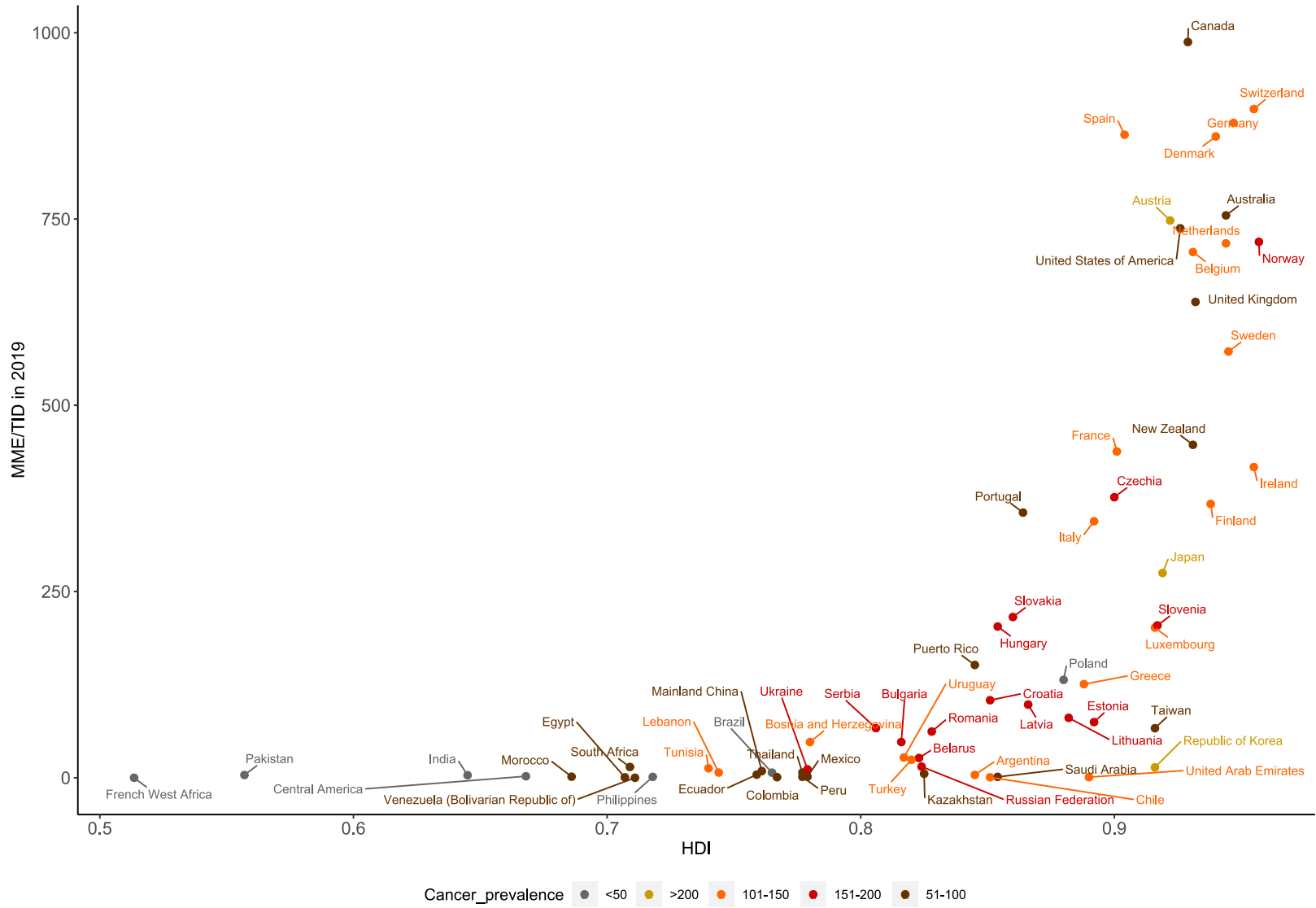
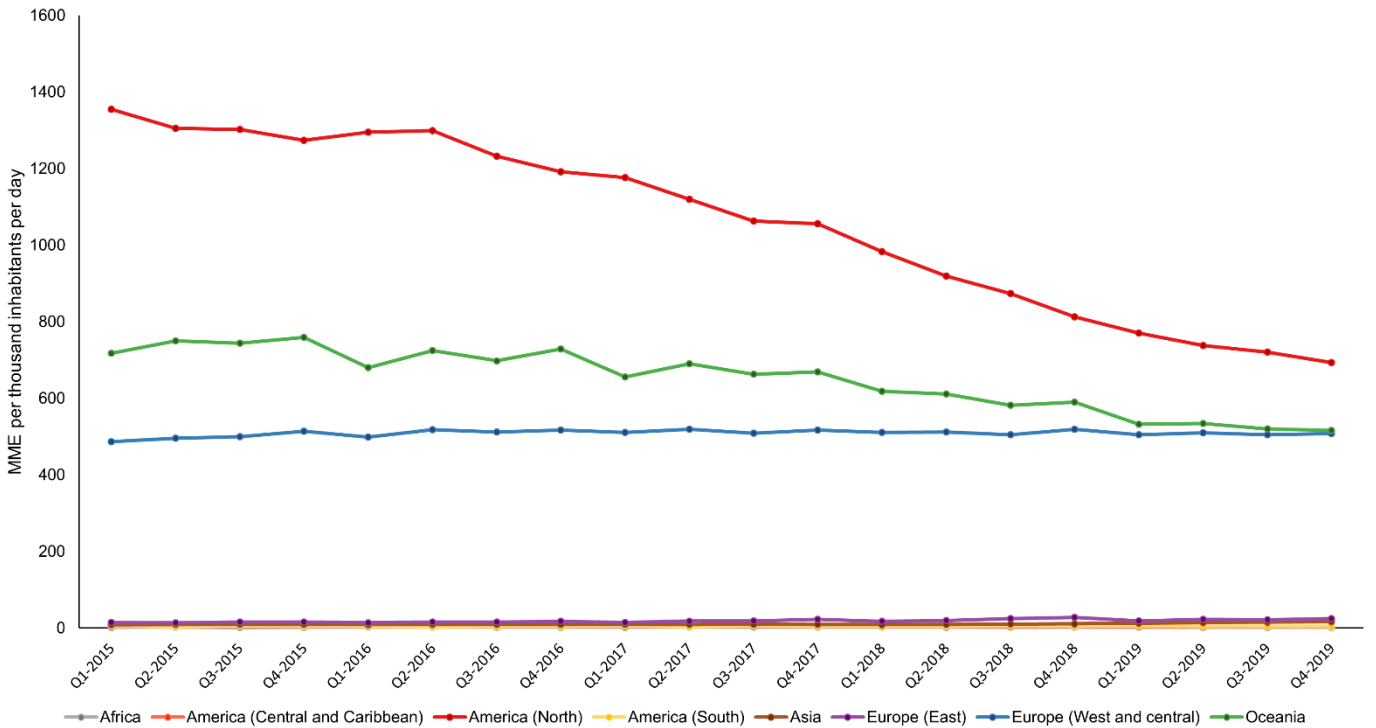


Figure S5. Scatter plot of opioid analgesic consumption and Human Development Index (HDI) by cancer prevalence.

(A) Trends in strong opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019



(B) Trends in strong opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019

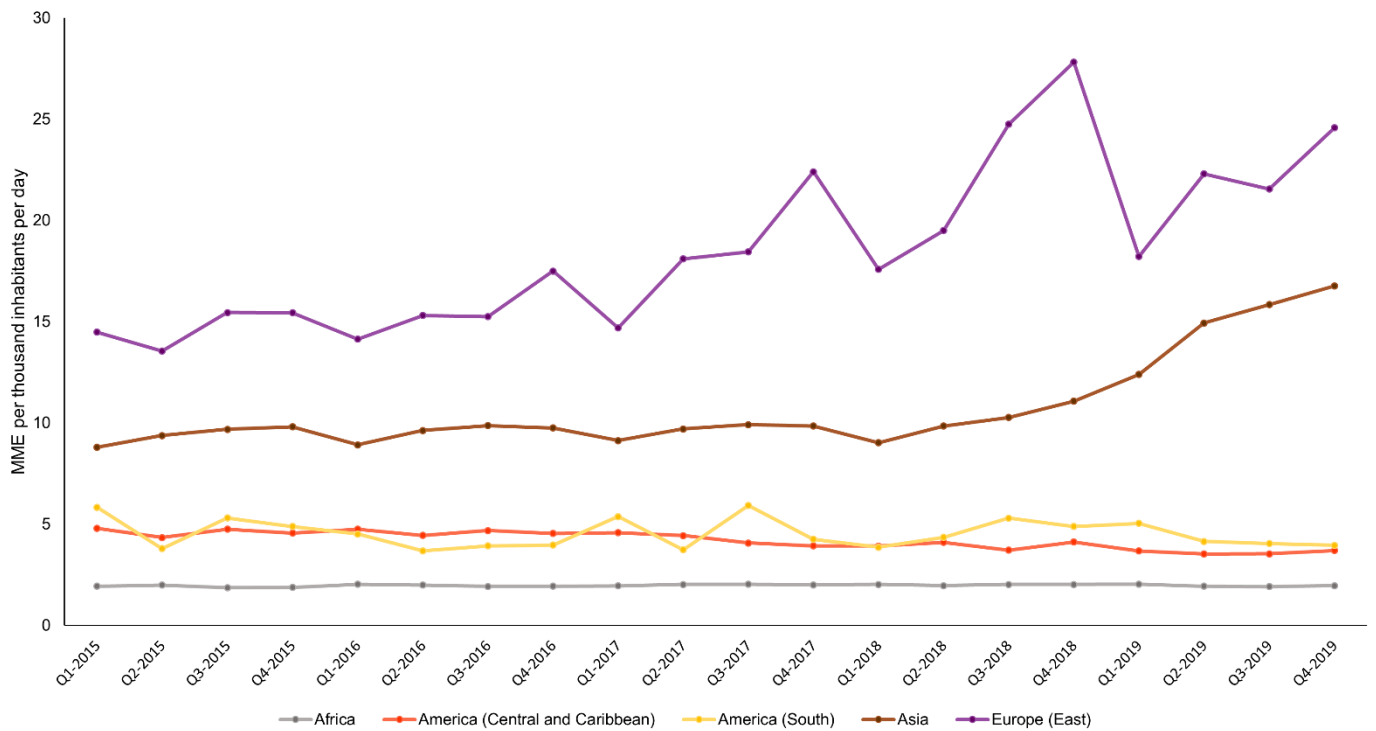
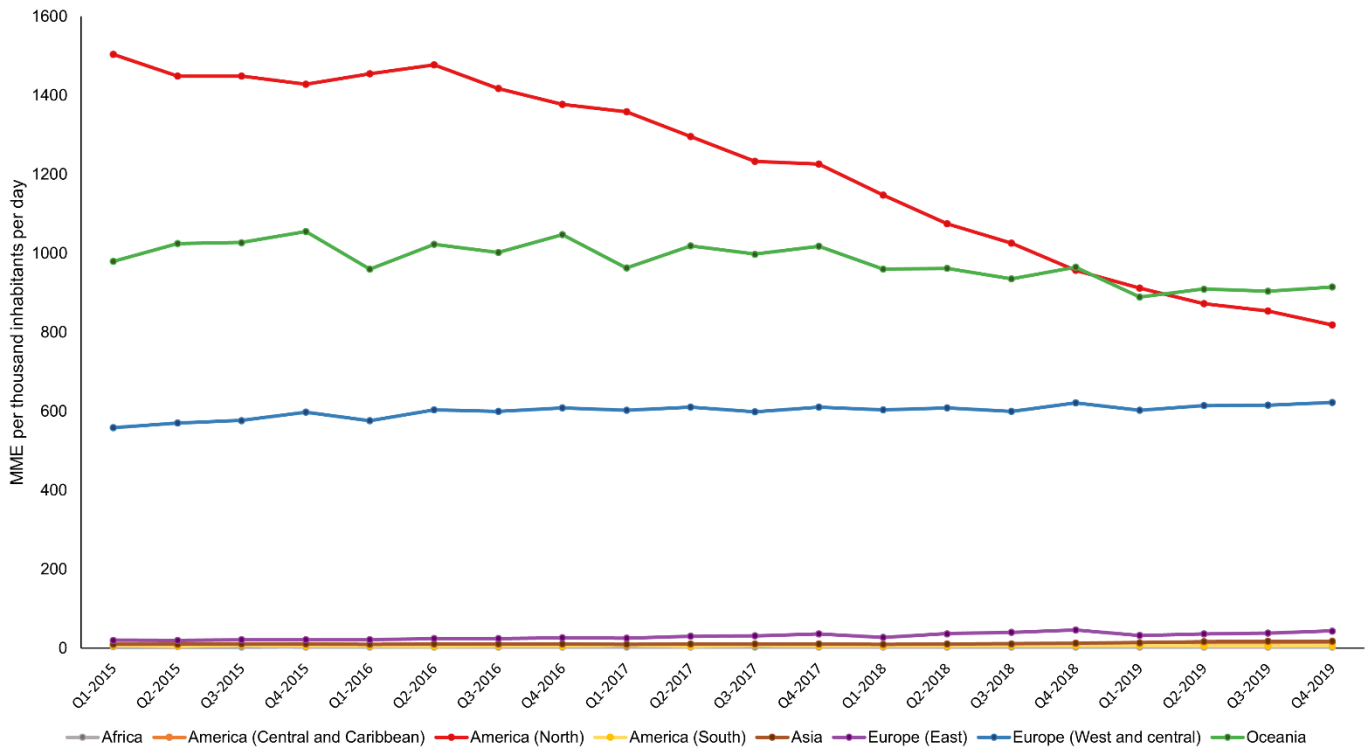


Figure S6. Sensitivity analysis: quarterly trends in strong opioid analgesic consumption at the regional level between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID.

MME: milligram morphine equivalent.

(A) Trends in opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019



(B) Trends in opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019

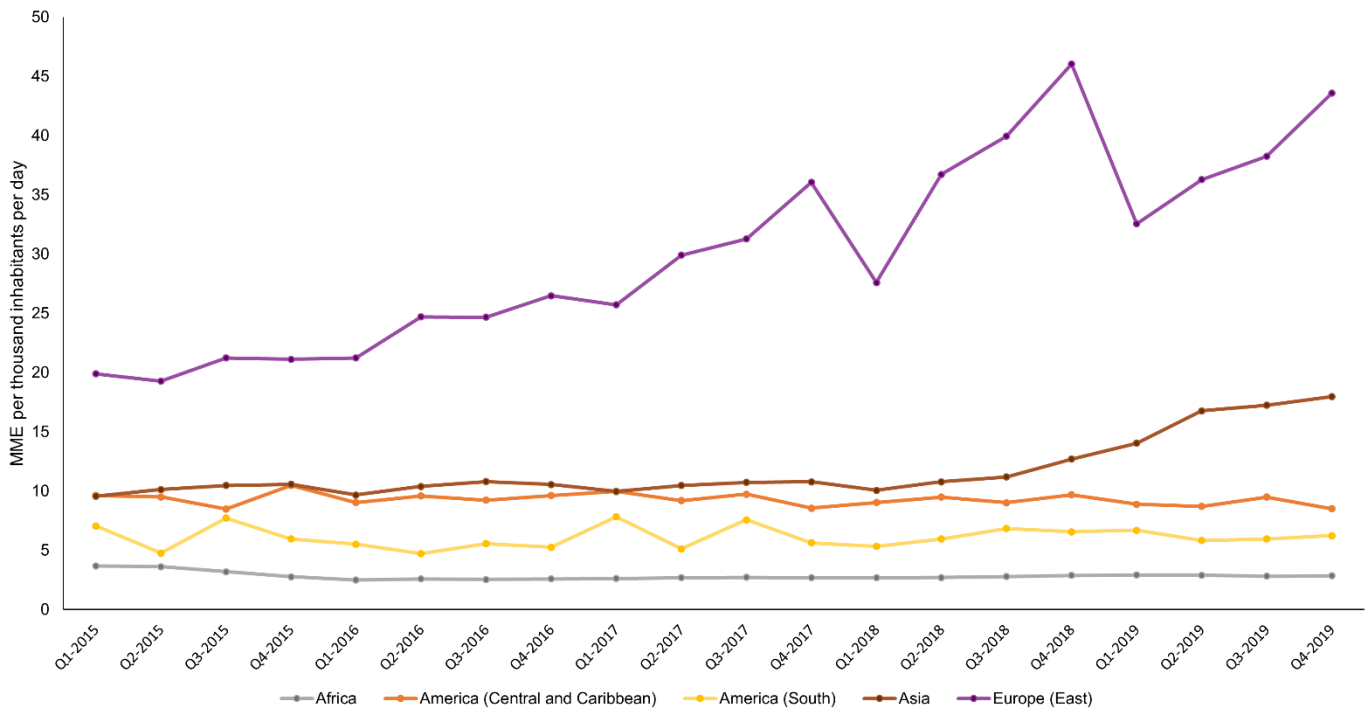
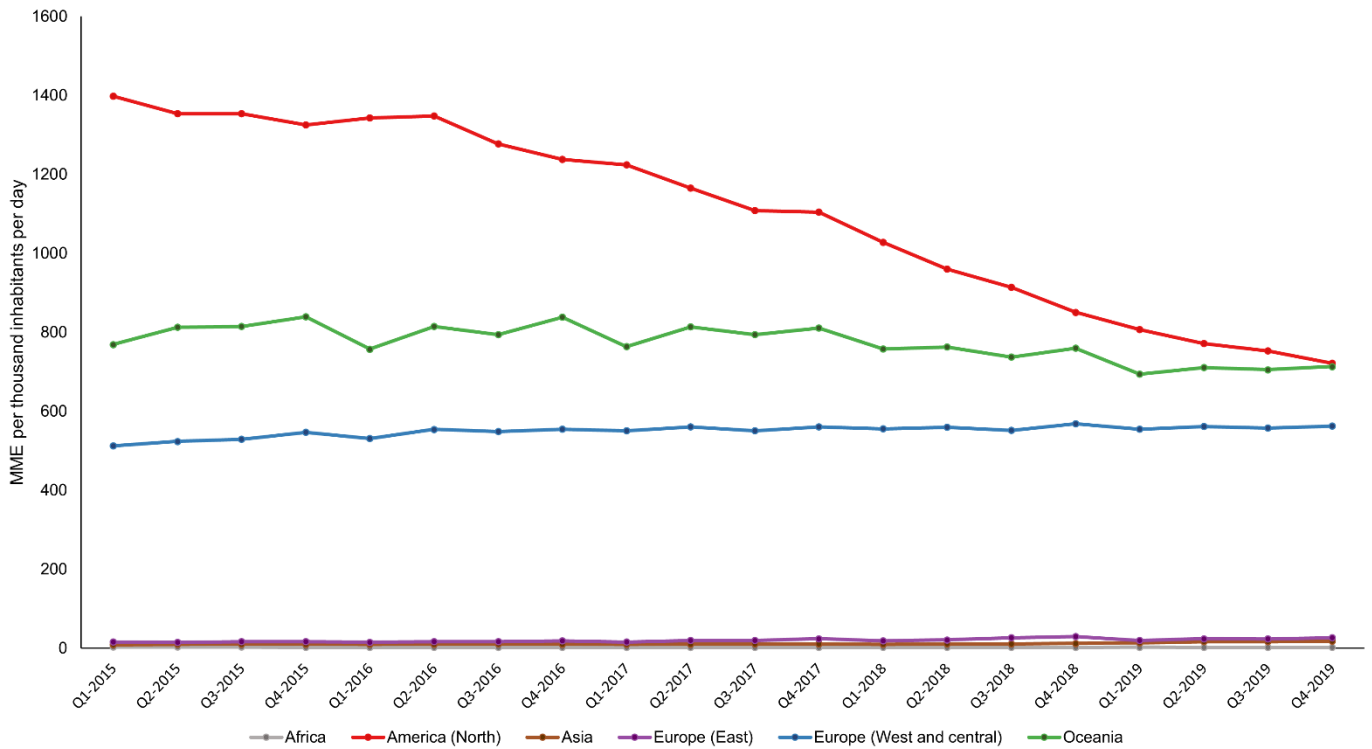


Figure S7. Sensitivity analysis: quarterly trends in opioid analgesic (including N02A buprenorphine, methadone, and levomethadone) consumption at the regional level between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID.

MME: milligram morphine equivalent.

(A) Trends in opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019



(B) Trends in opioid analgesic consumption in MME per 1,000 inhabitants per day, 2015-2019

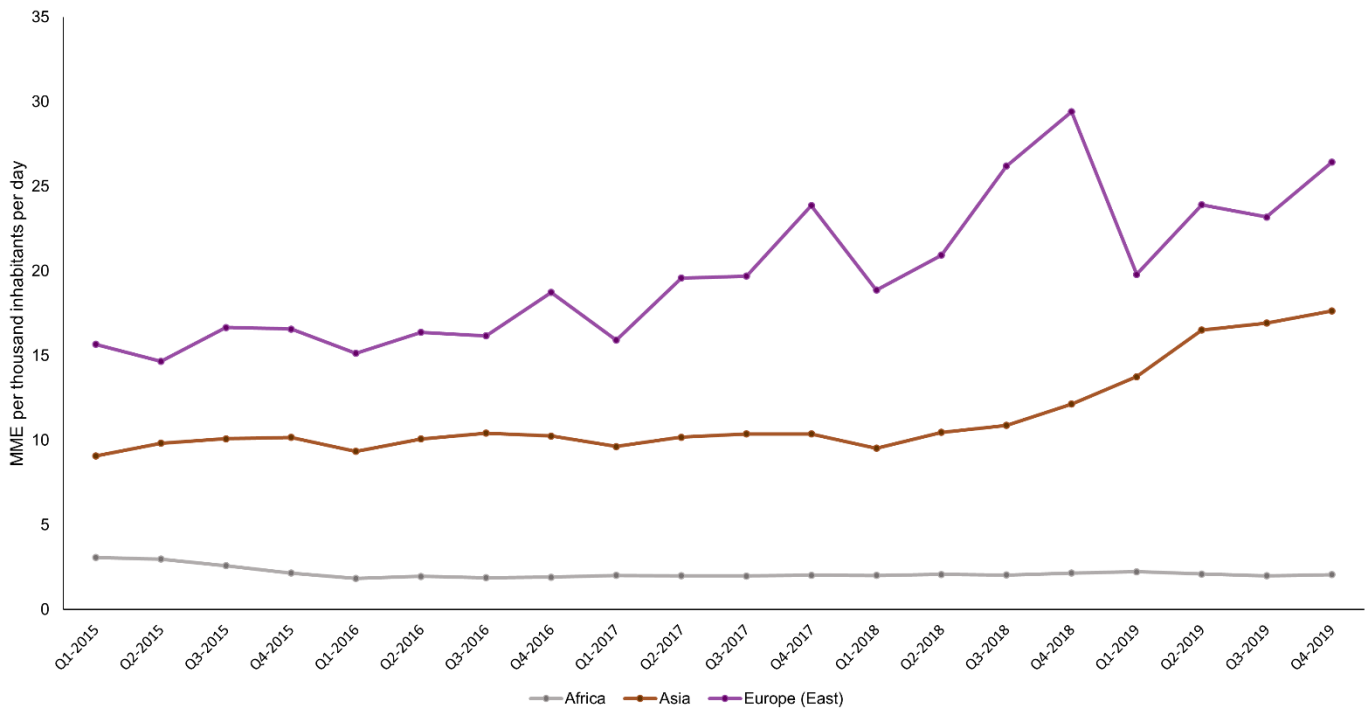


Figure S8. Sensitivity analysis: quarterly trends in opioid analgesic consumption at the regional level (only included countries with sales data available from both hospital and retail sectors) between 2015 to 2019, (A) all regions; (B) regions with less than 100 MME/TID.

MME: milligram morphine equivalent.

References:

1. Nations U. 2019 Revision of World Population Prospects. 2019. <https://population.un.org/wpp/> (accessed 28th June 2021).
2. Nations U. Human Development Reports, Human Development Index (HDI). 2019. <http://hdr.undp.org/en/home> (accessed 28th June 2021).
3. GDP per capita (current US\$). 2019. <https://data.worldbank.org/indicator/NY.GDP.PCAP.CD> (accessed 28th June 2021).
4. Knaul FM, Farmer PE, Krakauer EL, et al. Alleviating the access abyss in palliative care and pain relief—an imperative of universal health coverage: the Lancet Commission report. *The Lancet* 2018; **391**(10128): 1391-454.
5. Global Health Data Exchange. 2019. <http://ghdx.healthdata.org/> (accessed 28th June 2021).
6. Meijer DK, Hovinga G, Versluis A, et al. Pharmacokinetics of the oral narcotic analgesic bezitramide and preliminary observations on its effect on experimentally induced pain. *Eur J Clin Pharmacol* 1984; **27**(5): 615-8.
7. Opioid morphine equivalent conversion factor: Centers for Medicare & Medicaid Services, 2017.
8. Curtis HJ, Croker R, Walker AJ, Richards GC, Quinlan J, Goldacre B. Opioid prescribing trends and geographical variation in England, 1998–2018: a retrospective database study. *The Lancet Psychiatry* 2019; **6**(2): 140-50.
9. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. *Pharmacoepidemiol Drug Saf* 2016; **25**(6): 733-7.
10. Nissen SK, Pottegard A, Ryg J. Trends of Opioid Utilisation in Denmark: A Nationwide Study. *Drugs Real World Outcomes* 2019; **6**(4): 155-64.
11. Luchting B, Rachinger-Adam B, Hulde N, Heyn J, Azad SC. Challenging equipotency calculation for hydromorphone after long-term intravenous application. *Ann Palliat Med* 2017; **6**(Suppl 1): S90-S4.
12. Prommer E. Levorphanol: the forgotten opioid. *Support Care Cancer* 2007; **15**(3): 259-64.
13. Bekkering GE, Soares-Weiser K, Reid K, et al. Can morphine still be considered to be the standard for treating chronic pain? A systematic review including pair-wise and network meta-analyses. *Curr Med Res Opin* 2011; **27**(7): 1477-91.
14. Berdine HJ, Nesbit SA. Equianalgesic Dosing of Opioids. *Journal of Pain & Palliative Care Pharmacotherapy* 2009; **20**(4): 79-84.
15. Mercadante S. The role of tapentadol as a strong opioid in cancer pain management: a systematic and critical review. *Curr Med Res Opin* 2017; **33**(11): 1965-9.
16. Schulz R, Blasig J, Wuster M, Herz A. The opiate-like action of tilidine is mediated by metabolites. *Naunyn Schmiedebergs Arch Pharmacol* 1978; **304**(2): 89-93.
17. Bender KI, Gerasimova OV. [Relationship between the pain-relieving action of narcotic analgesics and their effect on respiration]. *Farmakol Toksikol* 1976; **39**(5): 552-6.