Timing of launches of essential medicines across the world: 1982-2024

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GLOBAL HEALTH POLICY

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Low- And Middle-Income Countries Experienced Delays Accessing New Essential Medicines, 1982–2024

Health Affairs, 43, 1410–1419 (October 2024).

Research questions

- From the time they first become available to patients anywhere in the world, how long does it take for essential medicines to become available in different countries?
- How do these time vary by characteristics of medicines and of countries?

Data

- Purchased from IQVIA
- 119 medicines (or groups of listed alternatives) on the 2023 WHO Essential Medicines List
  - all that first became available ("launched") somewhere from 1/1982 onwards
  - ...except for medicines for HIV/AIDS, TB, malaria, Ebola, and neglected tropical diseases
- Recorded launches in 75 markets (representing 90 countries)

Example: Simvastatin

- Included in the EML since 2007, for treating Mixed hyperlipidaemia and Coronary atherosclerosis
  - with four therapeutic alternatives: atorvastatin, paravastatin, fluvastatin, lovastatin
- Launches:
  - 1st in the US, 9/1987
  - has by now been launched in all of these markets
    (except that observation for Vietnam is missing)
  - last among these markets was Bangladesh, 1/1999
- Median time to launch across the markets: 2.2 years.

Outcome of interest

Time (in months) from first launch somewhere to launch in each country

- follow-up time up to a date in late 2023 or early 2024 in most countries
- regarded as censored if not launched by end of follow-up
- 6871 observed launches, 87% of possible launches for this sample (and thus 13% censored)

Notation

- Y_{ij}: time for drug i from first launch to launch in market j
- Distribution of Y_{ij}:
  - $F_{ij}(y) = 1 - S_{ij}(y) = P(Y_{ij} \leq y)$: cumulative distribution function.
  - $h_{ij}(y)$: hazard function
- ... conditional on (some or all of) covariates $\mathbf{W}_{ij}(t) = (\mathbf{X}_i, \mathbf{Z}_j(t))$
  - medicine-level covariates $\mathbf{X}_i$
  - market-level covariates $\mathbf{Z}_j(t)$, which may be time-varying

Covariates

Medicine-level covariates:

- Clinical category: antibiotics, cancer drugs, cardiovascular drugs, or other
- Decade of first launch: 1982–89, 1990–99, 2000–09, or 2010–20

Market-level covariates:

- Income group (World Bank): Low, Lower Middle, Upper Middle, High
  - modal value over the observation period (time-constant), or (in a supplementary analysis) annual value (time-varying)
- macro region
- log population size (time-varying)
- log GDP per capita (time-varying)

Methods 1: Regression modelling

- Proportional hazards model (Cox model) for hazard $h_{ij}(y)$.
- Allowing for the fact that the data are clustered in two (cross-classified) ways: by drug and by market.
  - We do this by stratification (i.e. separate baseline hazards) by one, and estimated standard errors clustered by the other
- Models given drug-level covariates:

$$h_{ij}(y) = h_{0j}(y) \exp(\beta_x \mathbf{X}_i)$$

  stratified by market j, and standard errors clustered by drug i
- ... or models given market-level covariates:

$$h_{ij}(y) = h_{0i}(y) \exp(\beta_w \mathbf{W}_j(y))$$

  stratified by drug i, and standard errors clustered by market j.

Example: A model given market-level covariates

	P value	Coefficient est.	(se)	Hazard ratio est.	(95% CI)
log GDP per capita	<0.001	0.418	(0.059)	1.519	(1.353, 1.706)
WHO region (vs. Europe)	<0.001				
Africa		-0.554	(0.327)	0.575	(0.303, 1.090)
Americas		-0.138	(0.124)	0.871	(0.683, 1.111)
Eastern Mediterranean		-0.729	(0.113)	0.482	(0.386, 0.602)
South East Asia		-0.367	(0.288)	0.693	(0.394, 1.219)
Western Pacific		-0.442	(0.192)	0.643	(0.441, 0.936)
Logarithm of population size (time-varying)	0.006	0.121	(0.044)	1.129	(1.035, 1.231)

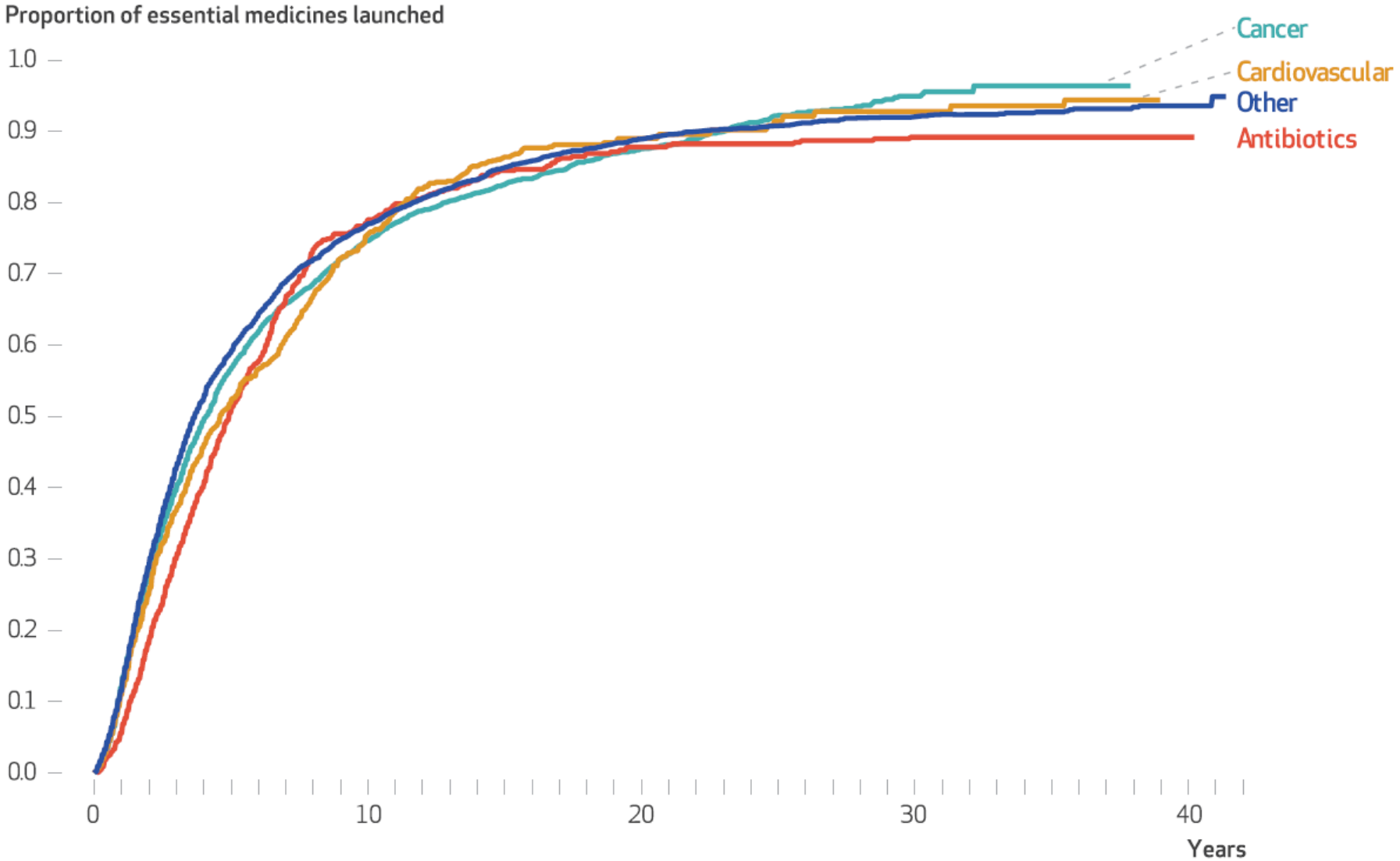
Methods 2: Estimates of distributions of times to launch

- Kaplan-Meier estimates of $F_{ij}(y) = 1 - S_{ij(y)}$ given different values of categorical covariates
  - and, from these, estimates of (say) median times to launch
- Log-rank tests of equal hazard functions $h_{ij}(y)$ given different values of categorical covariates
  - with p-values evaluated over random permutations of values of the covariates to the clusters (drugs or markets)

Example of comparisons: Clinical categories of drugs

EXHIBIT 2

Cumulative proportion of essential medicines that launched over time, by clinical category of medicine, 1982–2024



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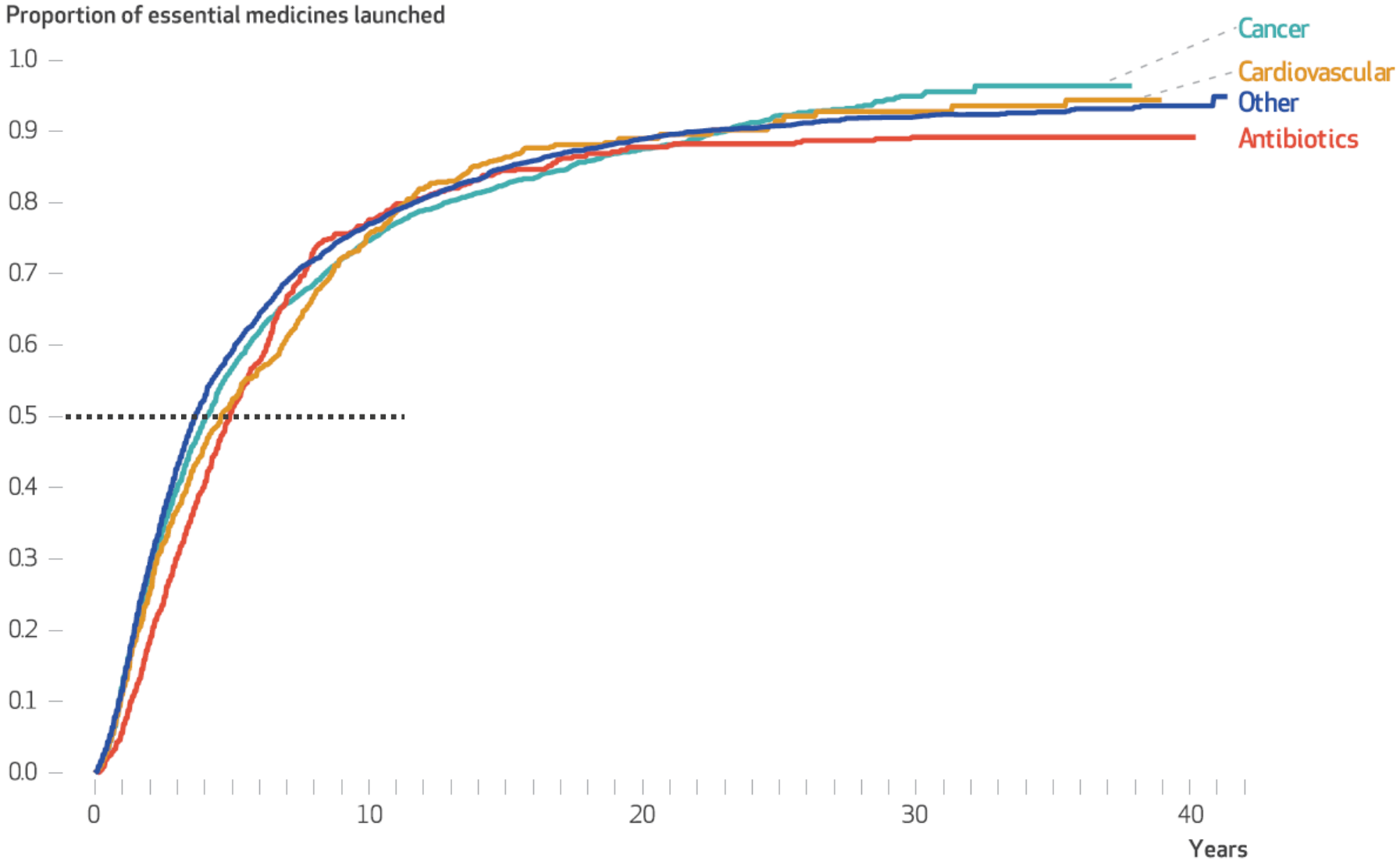


Median comparisons: Drug characteristics

DRUG CHARACTERISTICS		
Clinical category		
Antibiotics	16	4.9
Cancer	32	4.1
Cardiovascular	12	4.6
Other	59	3.7
Decade of first launch		
1982–89	37	5.4
1990–99	38	4.0
2000–09	29	3.2
2010–20	15	3.4

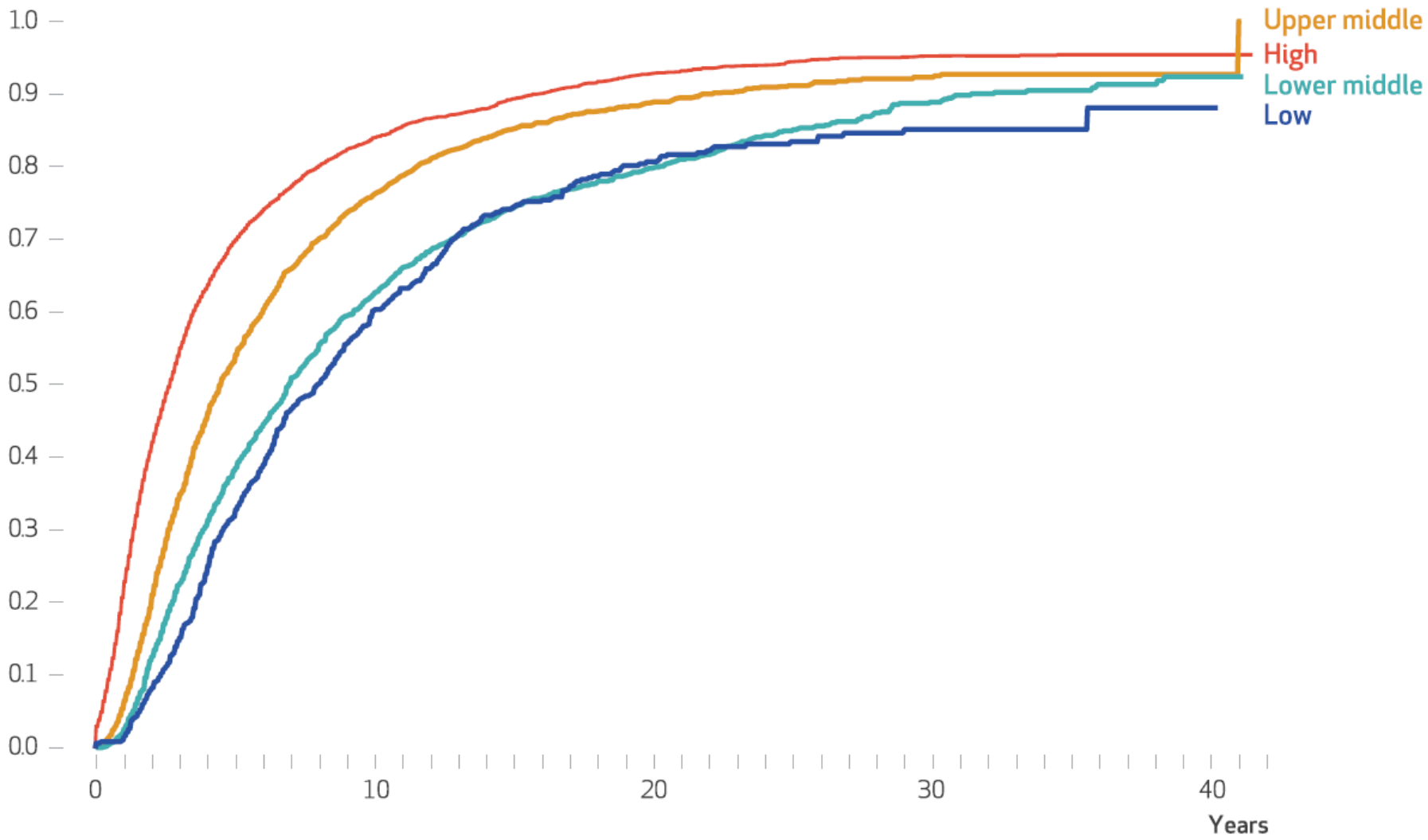
Median comparisons: WHO region

WHO region		
Africa	3	8.3
Americas	13	4.1
Eastern Mediterranean	9	7.8
Europe	34	2.9
South-East Asia	5	6.8
Western Pacific	11	3.5

The main comparison: Markets by income group

EXHIBIT 4

Cumulative proportion of essential medicines that launched over time, by income group of countries, 1982–2024

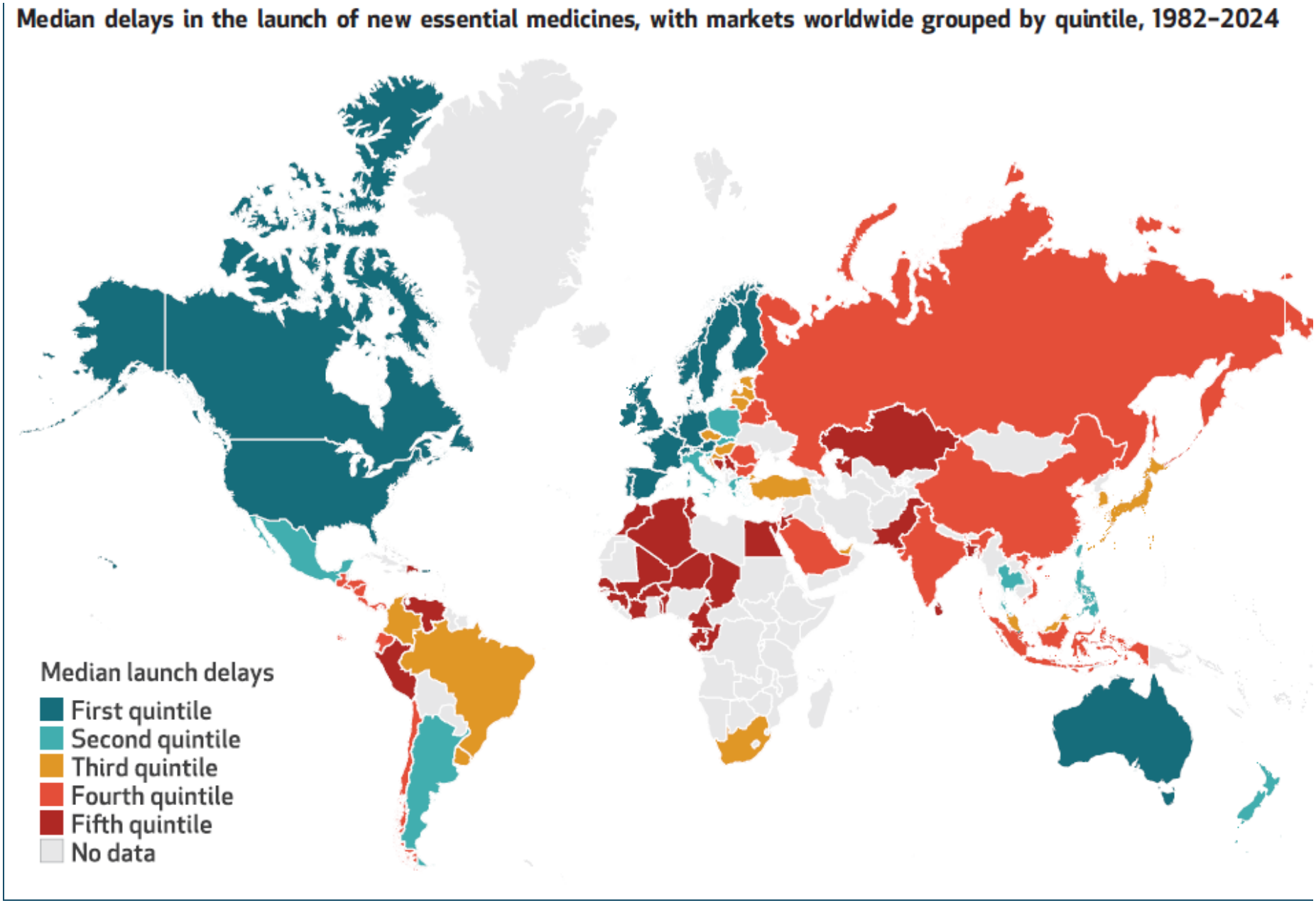


The main comparison: Markets by income group

Median time to launch of a new essential medicine, in years, by market and drug characteristics, 1982–2024

	No. of markets or drugs	Median (years)
MARKET CHARACTERISTICS		
World Bank income classification		
High income	36	2.7
Upper middle income	20	4.5
Lower middle income	14	6.9
Low income	5	8.0

The main comparison: Markets by income group



Interactions: Income group differences over time

	Decade of first launch			
	1982 -1989	*1990 -1999*	*2000 -2009*	*2010 -2020*
High income	4.0	2.9	1.8	1.4
Upper middle income	6.0	4.3	3.6	4.6
Lower middle income	7.0	6.8	6.9	8.6
Low income	9.0	8.2	7.3	6.8