

Estimated cost-based generic prices for selected antihypertensive medicines

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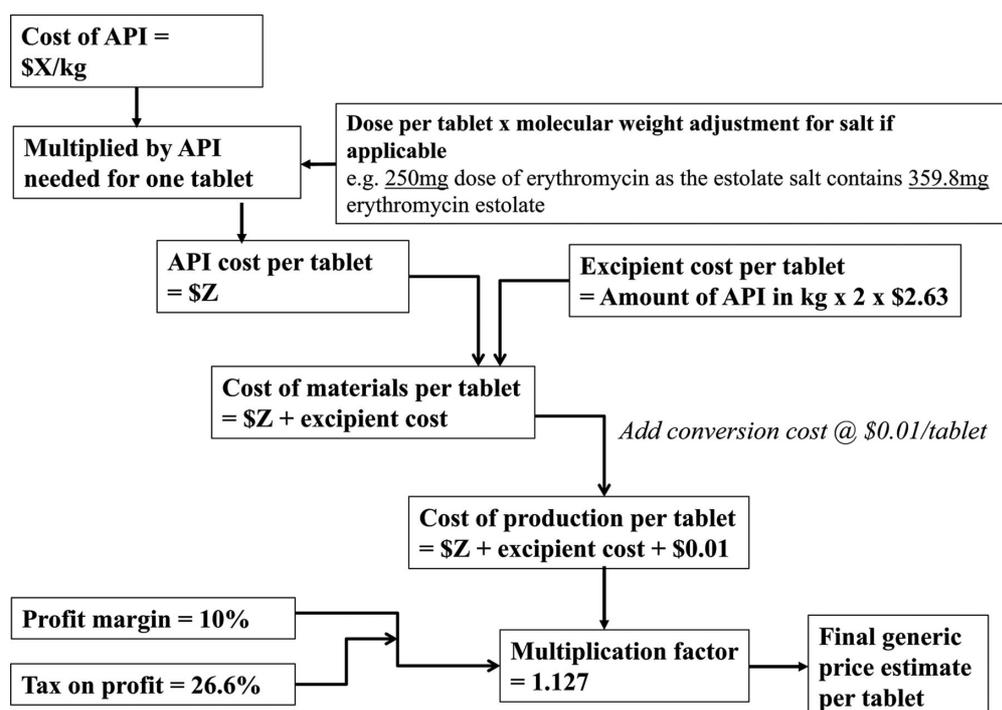
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1. Methodology

This analysis further develops a body of work on pharmaceutical costing. Cost-based estimates of manufacturing costs use real-world market data on active pharmaceutical ingredients (APIs). The costing methodology covers capital and operating expenses, taxation, and a profit margin. Detailed information on the methodology and assumptions can be found in the appendix to “Estimated costs of production and potential prices for the WHO Essential Medicines List” (*BMJ Global Health* 2018).ⁱ This method has been developed through a number of peer-reviewed studies on pharmaceutical cost of production, including for tuberculosis medicines,ⁱⁱ oralⁱⁱⁱ and injectable^{iv} medicines on the WHO Model List of Essential Medicines, insulins,^v hepatitis C^{vi} and HIV medicines,^{vii} and others.^{viii} The algorithm (Figure 1) estimates cost-based estimated generic prices, assuming competitive markets and a 10% profit margin.

Figure 1. Algorithm for cost-based estimated generic prices for solid oral dosage formulations



2. API

Data on the cost of active pharmaceutical ingredients (APIs) for amlodipine, hydrochlorothiazide, losartan, and telmisartan were extracted from an online database of import-export customs declarations (Panjiva). API exported from India from 1 January 2019 - 31 October 2021 (the most recent available data) were included. Manufacture in India was assumed due to the high quality of data available and the importance of India in global API and FFP pharmaceutical markets. Each record includes a short description of the goods exported, quantity, unit (e.g. kilograms or boxes), date, value, and information about the shipper and recipient. The search was conducted 18 December 2021, with queries “losartan”, “amlodipine”, “telmisartan”, and “hydrochlorothiazide”, respectively. Data were manually cleaned, and records that did not represent genuine API were excluded (Table 1, Figure 2).

Table 1. Criteria used for cleaning export data

Reason for censoring	Example of product description that would trigger censoring
Incorrect substance identified	“DIAMORPHINE” (in a search for “morphine”)
Item is part of a mix of products	“ABACAVIR, LOPINAVIR, LAMIVUDINE API”
Quantity of shipment < 1.0 kg, with exceptions made for very low-dose medicines	Value listed in “quantity” variable greater than 1.0kg
Finished Pharmaceutical Product (FPP), for example tablets	“Telmisartan Egis 80mg Tabs”
Impurity	“losartan impurity”
Unclear quantity of API	“TELMISARTAN DC GRANULES 12.5%” (In this example, the percentage descriptor could refer to a variety of parameters, for example, moisture content. As this is not specified, the true amount of API is unknown.)
Free sample or ‘no commercial value’	“ABACAVIR SULPHATE FREE SAMPLE” “ABACAVIR SULPHATE N.C.V.”
For veterinary use	“IVERMECTIN VETERINARY”
Reference/working standard	“Working Standard For Telmisartan (For sample Purpose Only)”

For some medicines, dosage is expressed as the dose of the active molecule, while the active pharmaceutical ingredient is sold as a salt form (e.g. one tablet of ‘10mg amlodipine’ contains 13.87mg of amlodipine besylate). The cost of per-unit API is adjusted as needed.

Data were cleaned in Microsoft Excel version 16.54. Statistical analyses and illustrations of active pharmaceutical ingredient export data were done in R version 4.1.2.

Figure 2. API data cleaning summary flowcharts

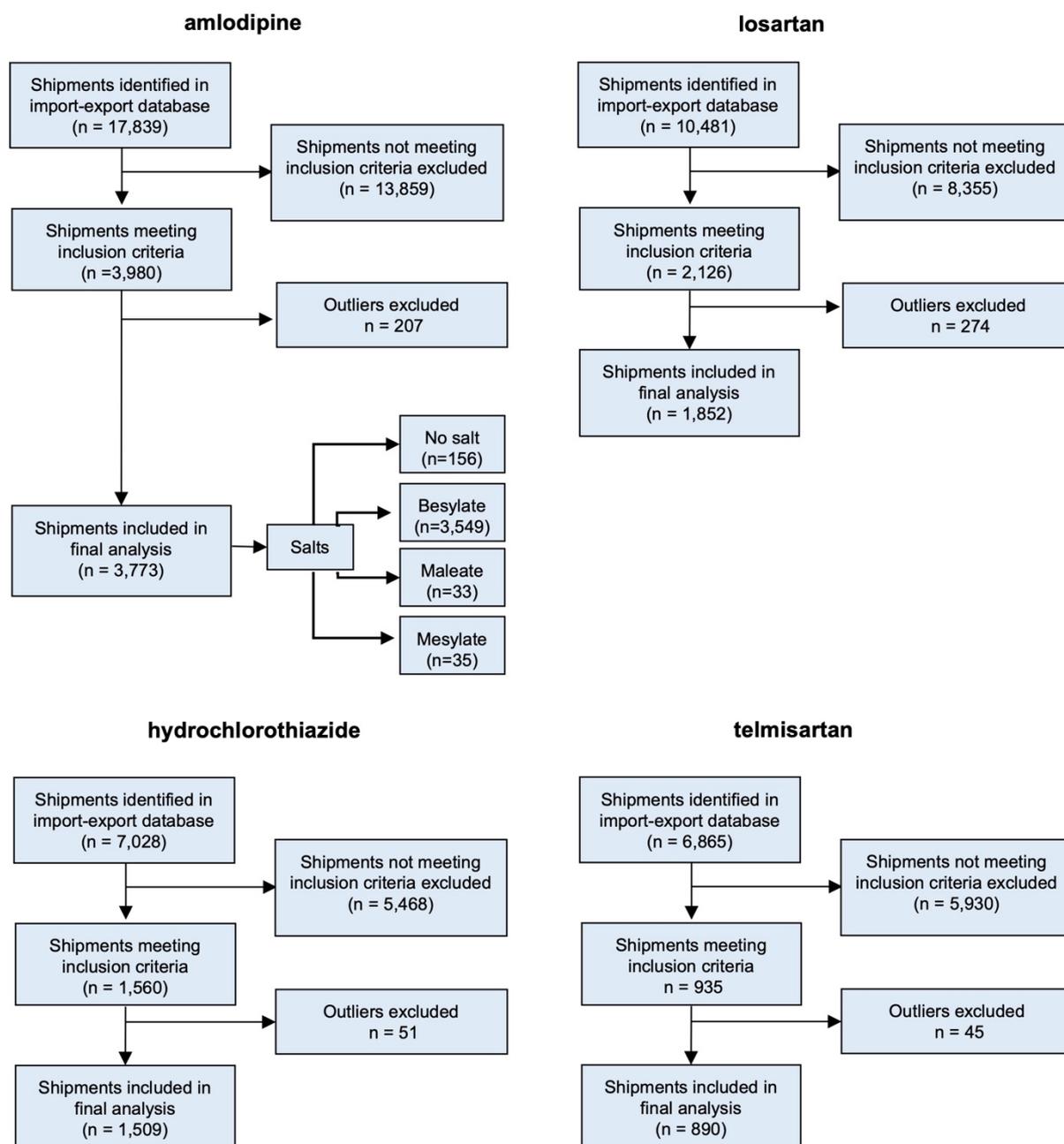


Table 2. Volume of exported API included in analysis after data cleaning

drug	volume
amlodipine	1,173,111
hydrochlorothiazide	582,545
losartan	1,941,821
telmisartan	323,043

3. Estimated cost-based generic prices for antihypertensive medicines

The weighted mean price per kilogram of active pharmaceutical ingredients (API) for selected antihypertensives ranged between US\$33 (HCTZ) to US\$328 (amlodipine, mesylate salt). See Table 3 for weighted averages by year, and for the last 12 months of data available (31 October 2020 - 2021).

Table 3. API price per kilogram, 2019- 2021

API		Price (US\$) per kg			
		2019	2020	2021 ¹	last 12 months
amlodipine	no salt/base/not specified	49.51	48.94	46.26	46.63
	besylate	89.91	87.37	90.29	91.05
	maleate	259.95	284.59	304.19	328.12
	mesylate	237.38	234.94	236.65	231.99
hydrochlorothiazide		32.57	32.83	33.27	33.30
losartan		99.69	98.70	84.32	86.12
telmisartan		166.73	175.32	152.06	153.59

Cost-based estimated generic prices of selected antihypertensive medicines were calculated according to methods described (Table 4). The API price used is weighted average cost per kg, 1 Nov 2020 – 31 Oct 2021. Where multiple salt forms exist, the most common salt was selected. Step-by-step visualizations are contained in Figures 3-7.

Table 4. Estimated cost-based generic price per tablet for selected antihypertensive medicines

Formulation (tablet)	Cost-based estimated generic price (US\$/tablet)
amlodipine 5mg	0.012
amlodipine 10mg	0.013
hydrochlorothiazide 12.5mg	0.012
hydrochlorothiazide 25mg	0.012

¹ 2021 data only available to 31 October 2021

losartan 25mg	0.014
losartan 50mg	0.017
losartan 100mg	0.023
telmisartan 40mg	0.018
telmisartan 80mg	0.026
losartan + amlodipine 50mg + 5mg	0.018
losartan + amlodipine 100mg + 5mg	0.023
losartan + amlodipine 100mg + 10mg	0.024
telmisartan + amlodipine 40mg + 5mg	0.019
telmisartan + amlodipine 80mg + 5mg	0.026
telmisartan + amlodipine 80mg + 10mg	0.027

Figure 3. Amlodipine 10mg tablet

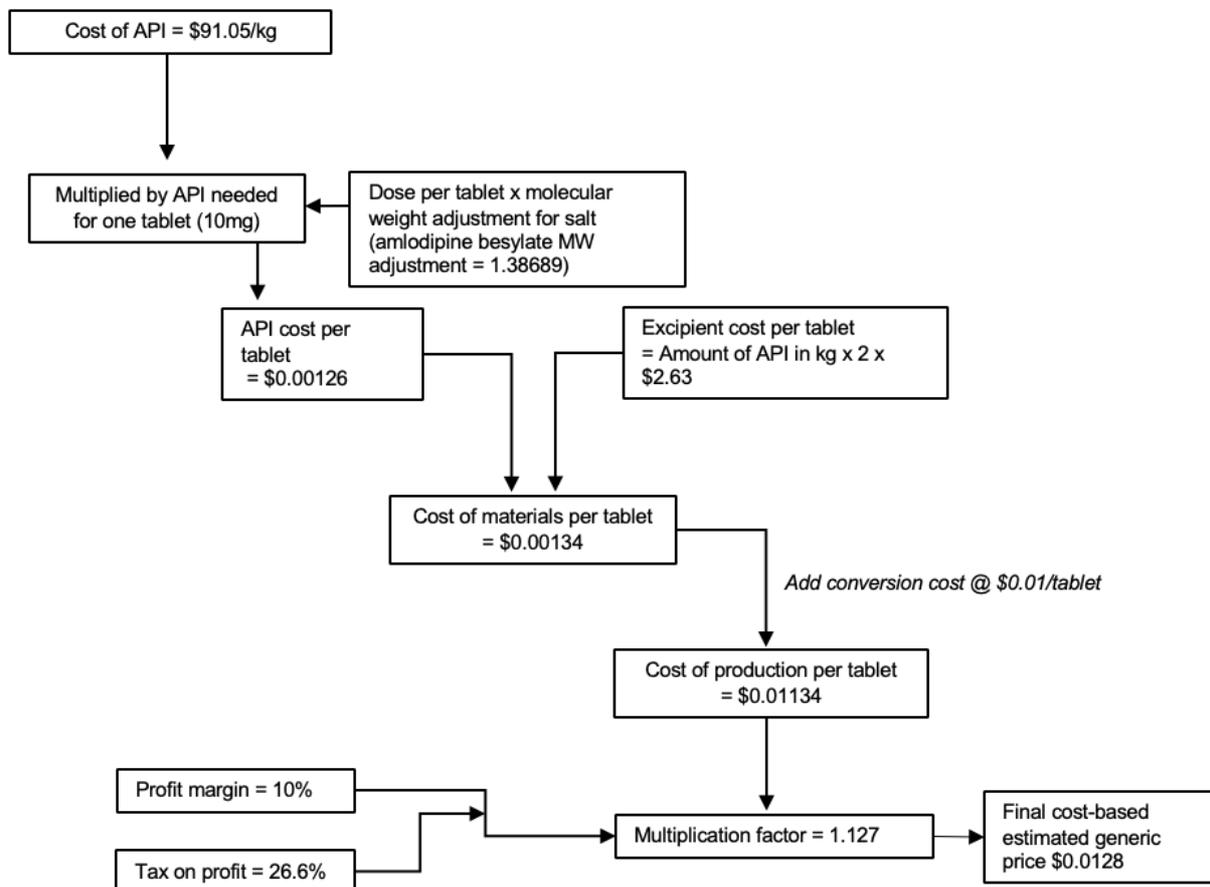


Figure 4. HCTZ 12.5mg tablet

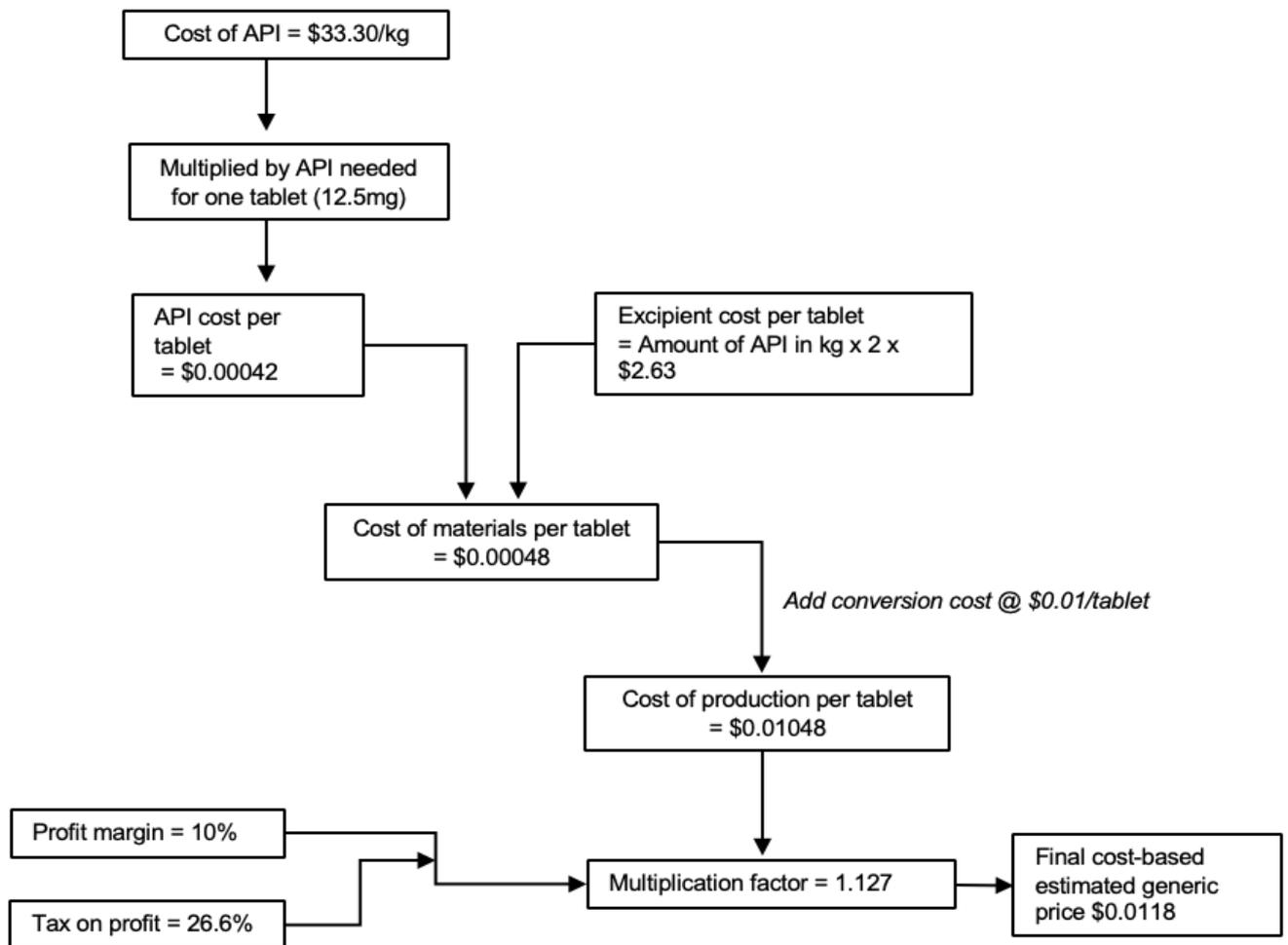


Figure 5. Losartan 50mg tablet

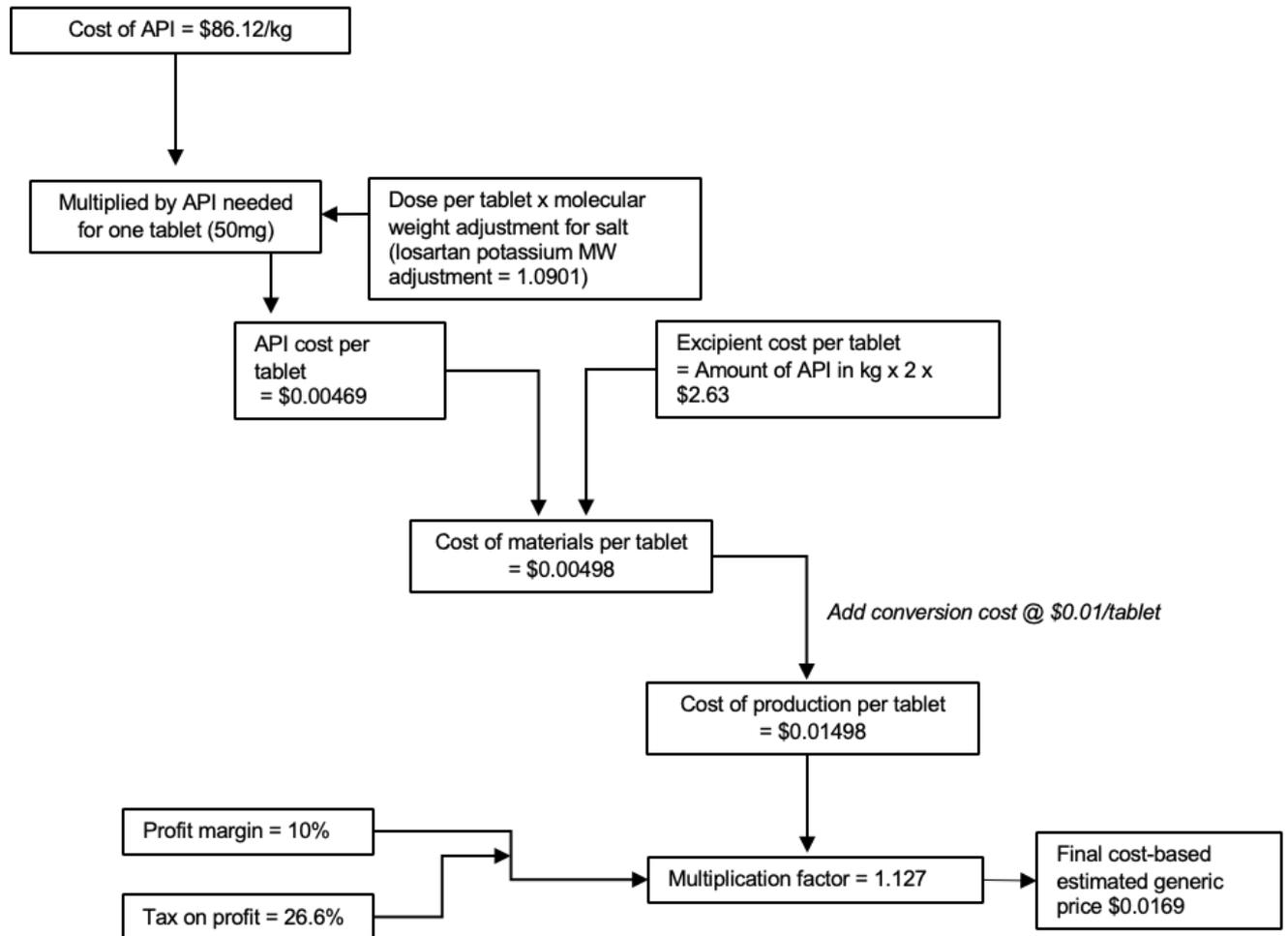


Figure 6. Telmisartan 40mg tablet

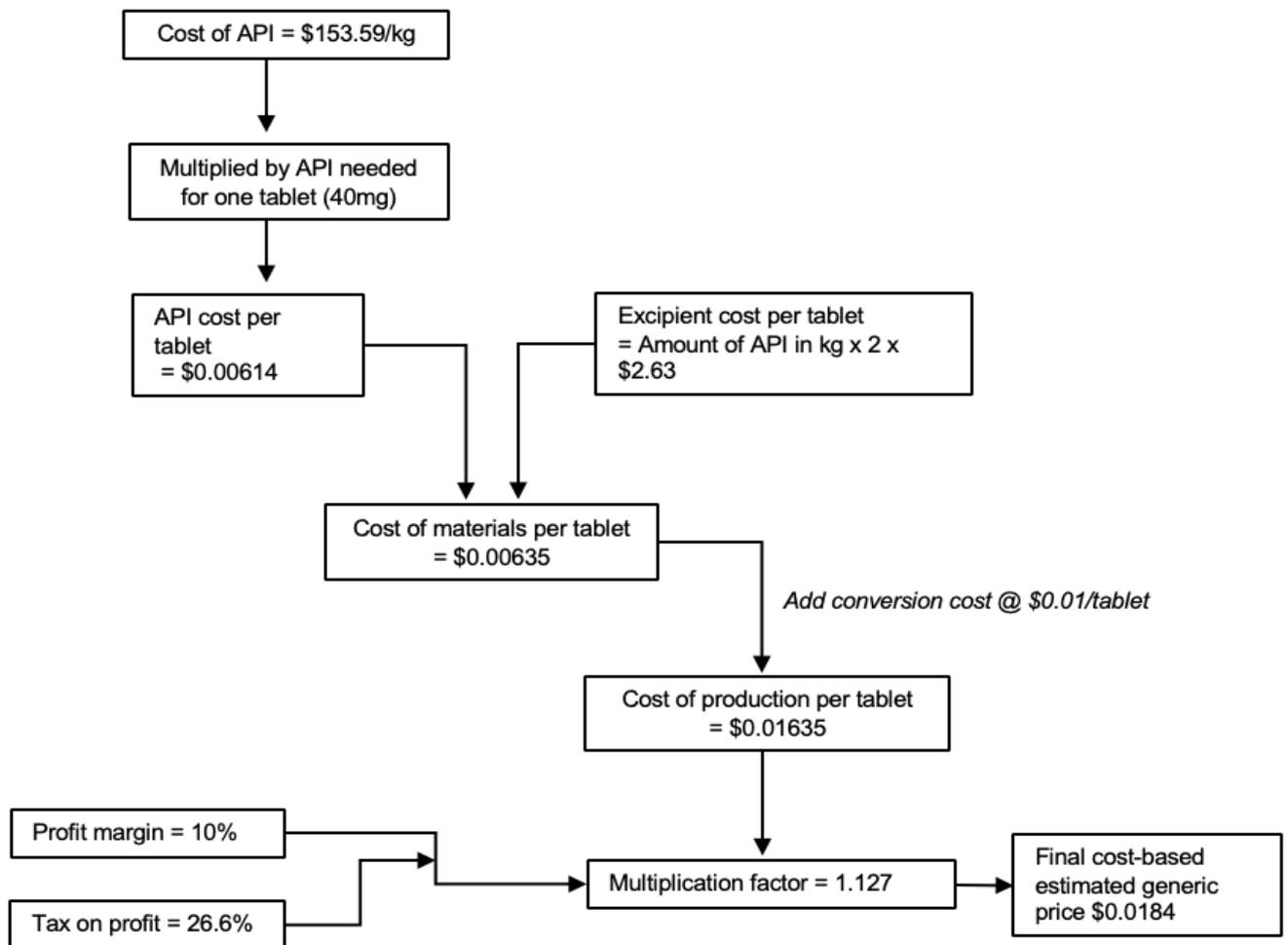
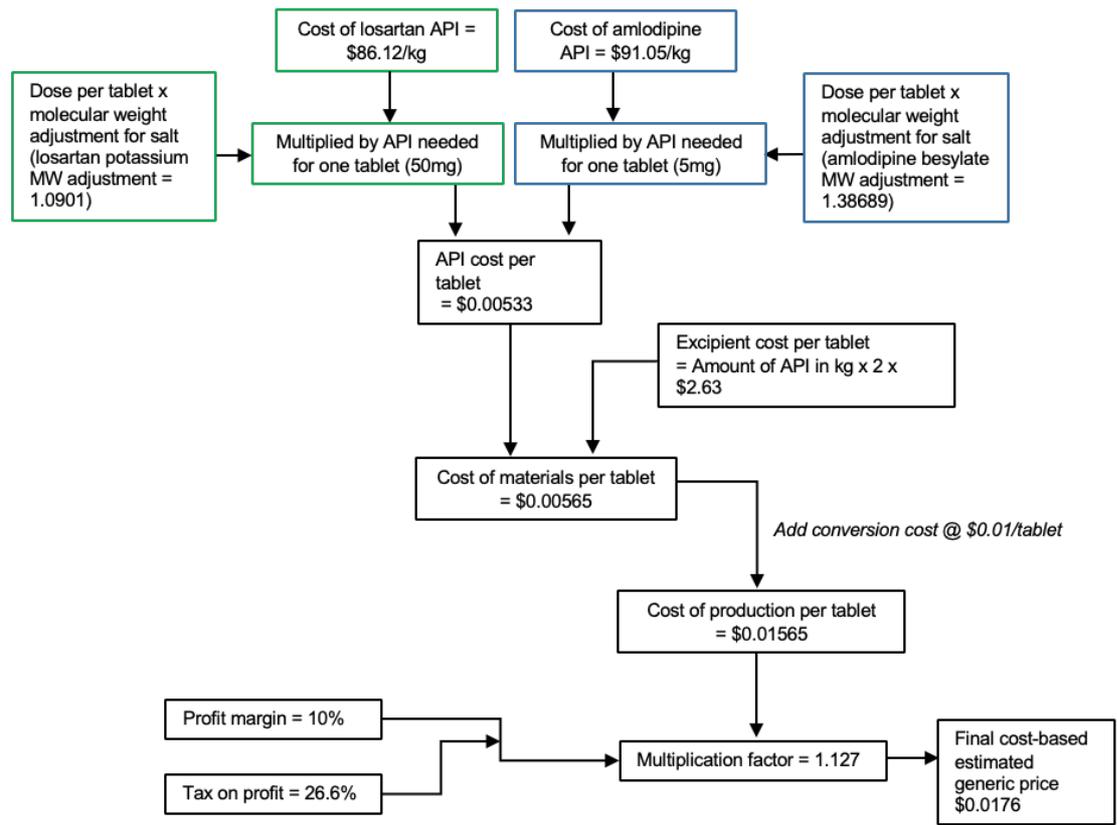


Figure 7. Losartan + amlodipine 50mg + 5mg tablet (FDC)



4. API change over time visualizations: linear regression

Scatter plots of API (Figures 8-14) with linear regressions (Table 5) visualize the change in price over time. The weighted linear regression includes Indian API export data from 1 Jan 2019 – 31 Oct 2021.

Table 5. Linear regression coefficients and estimated cost/kg 1 Nov 2021

drug	coefficient (change USD\$/kg per day)	coefficient (change USD\$/kg per year)	estimated US\$/kg value on 1 November 2021
amlodipine besylate	0.0021	0.75	90.15
amlodipine mesylate	-0.0052	-1.92	233.44
amlodipine maleate	0.0468	17.07	307.01
amlodipine no salt/base/not specified	-0.0045	-1.65	45.99
losartan potassium	-0.0229	-8.34	83.21
hydrochlorothiazide	0.0014	0.51	33.60
telmisartan	-0.0220	-8.04	159.41

Figure 8. Amlodipine besylate

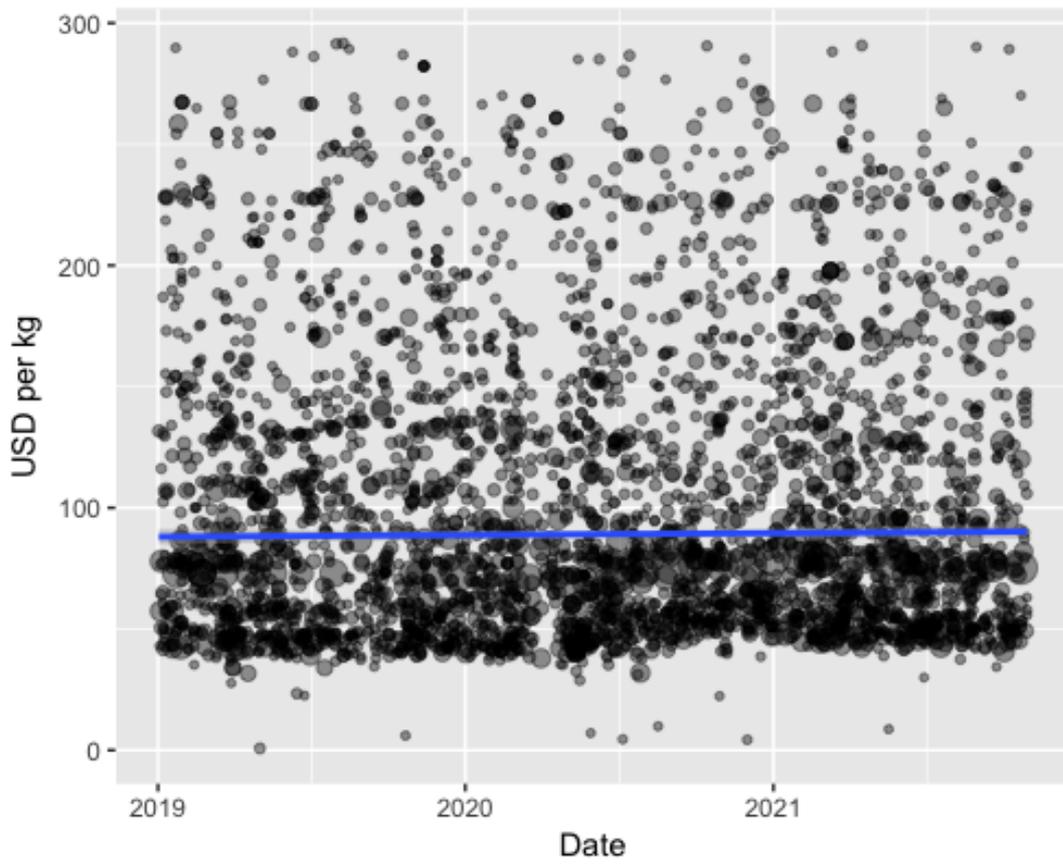


Figure 9. Amlodipine maleate

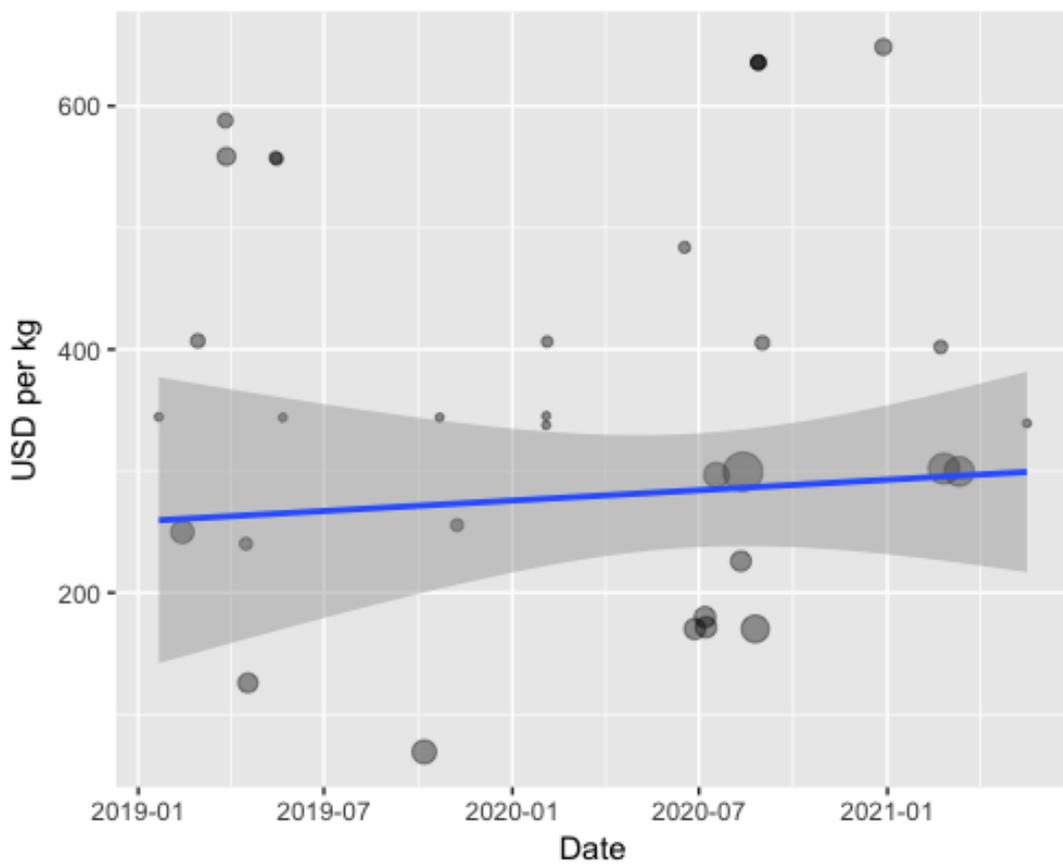


Figure 10. Amlodipine mesylate

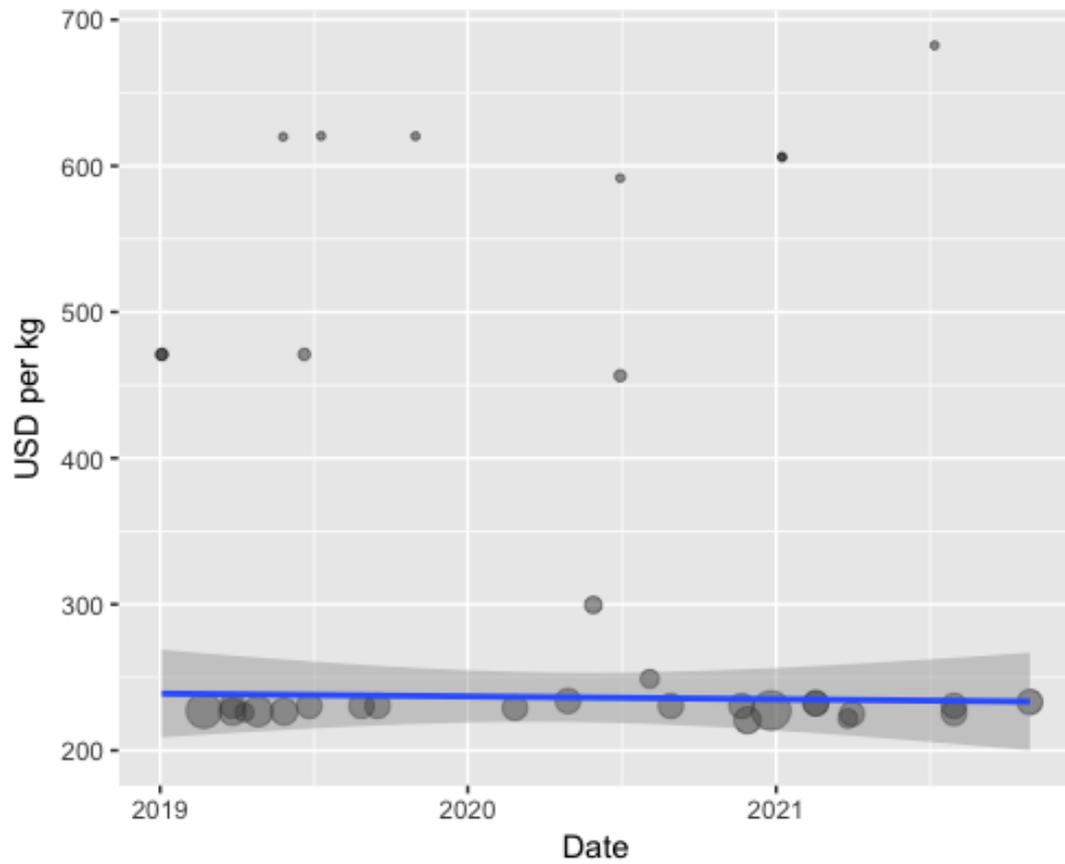


Figure 11. Amlodipine no salt/base/not specified

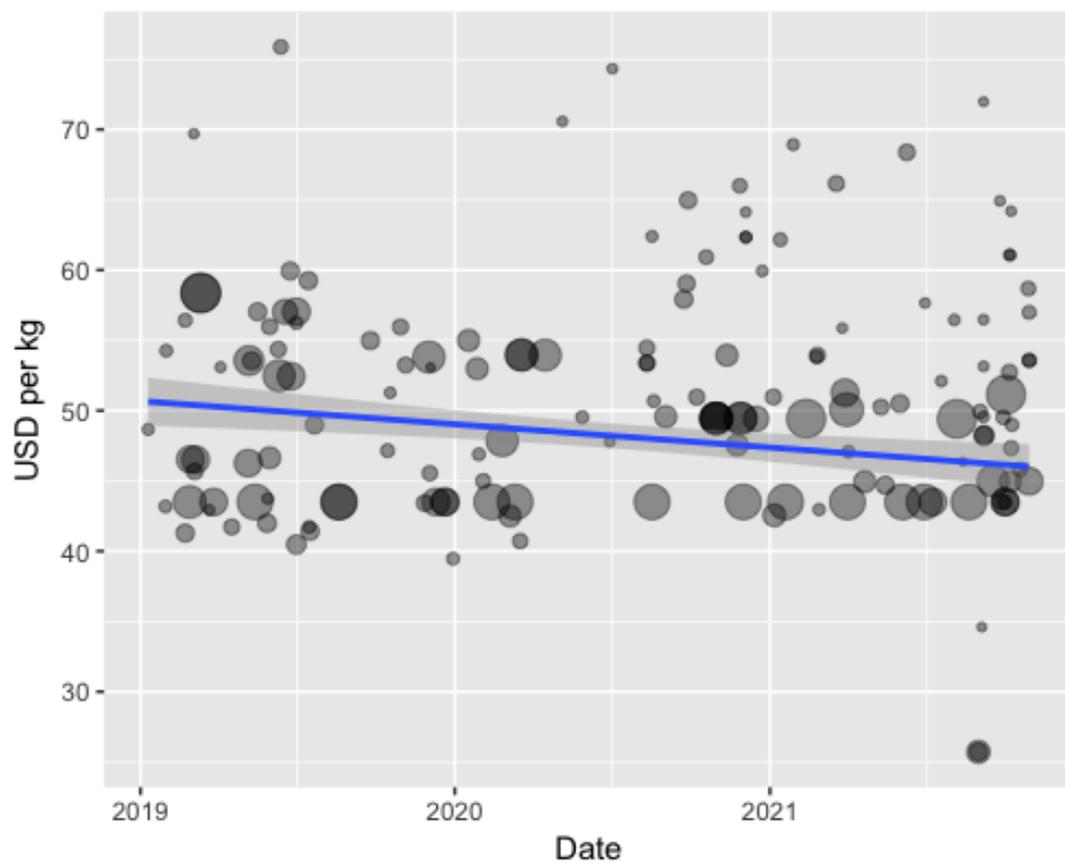


Figure 12. HCTZ

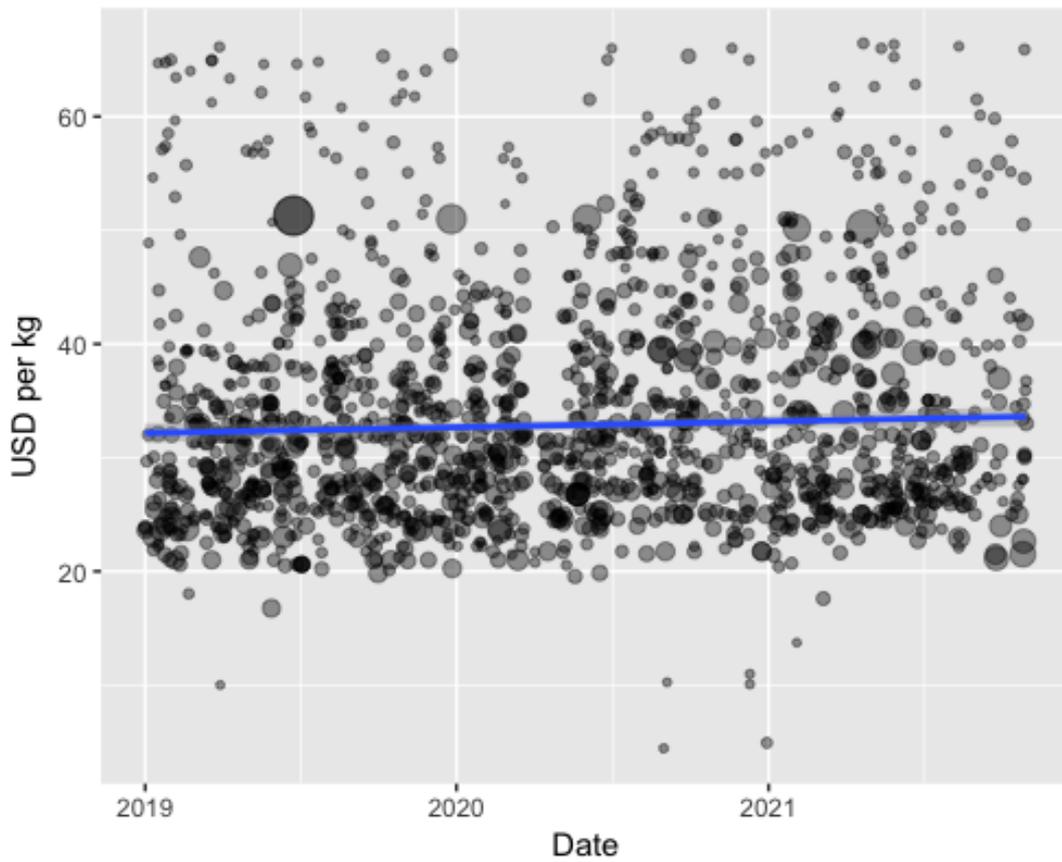


Figure 13. Losartan

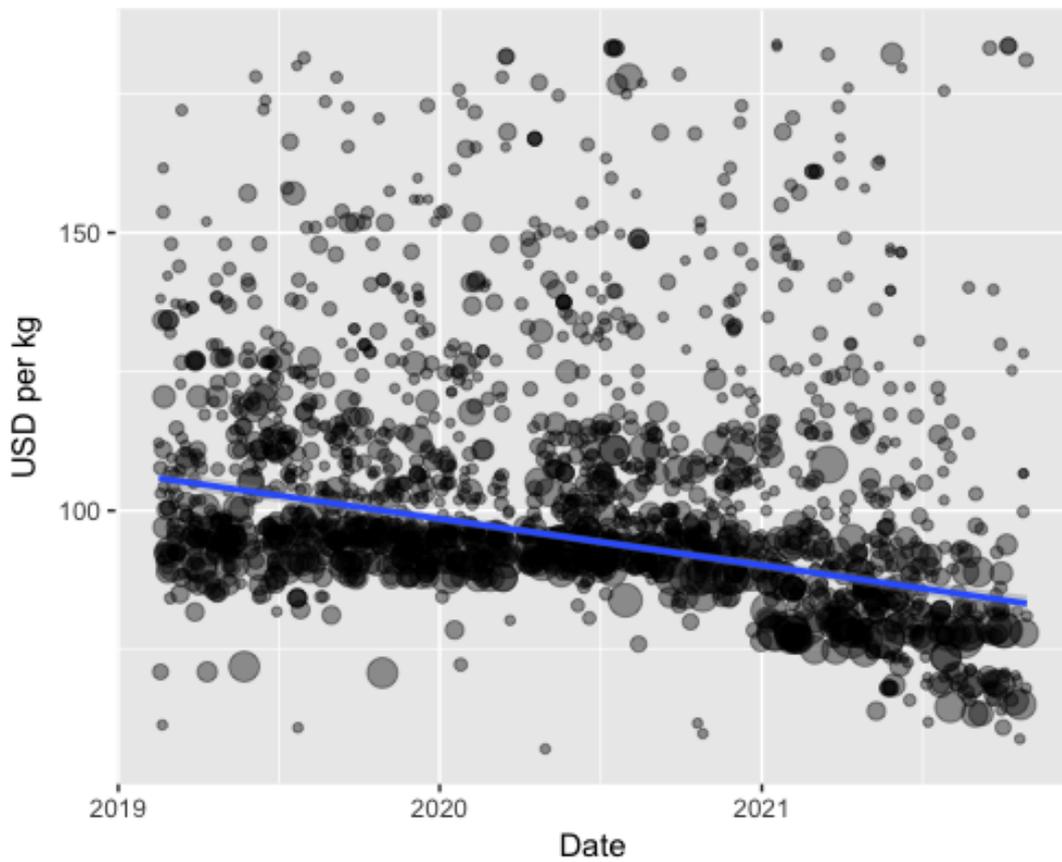
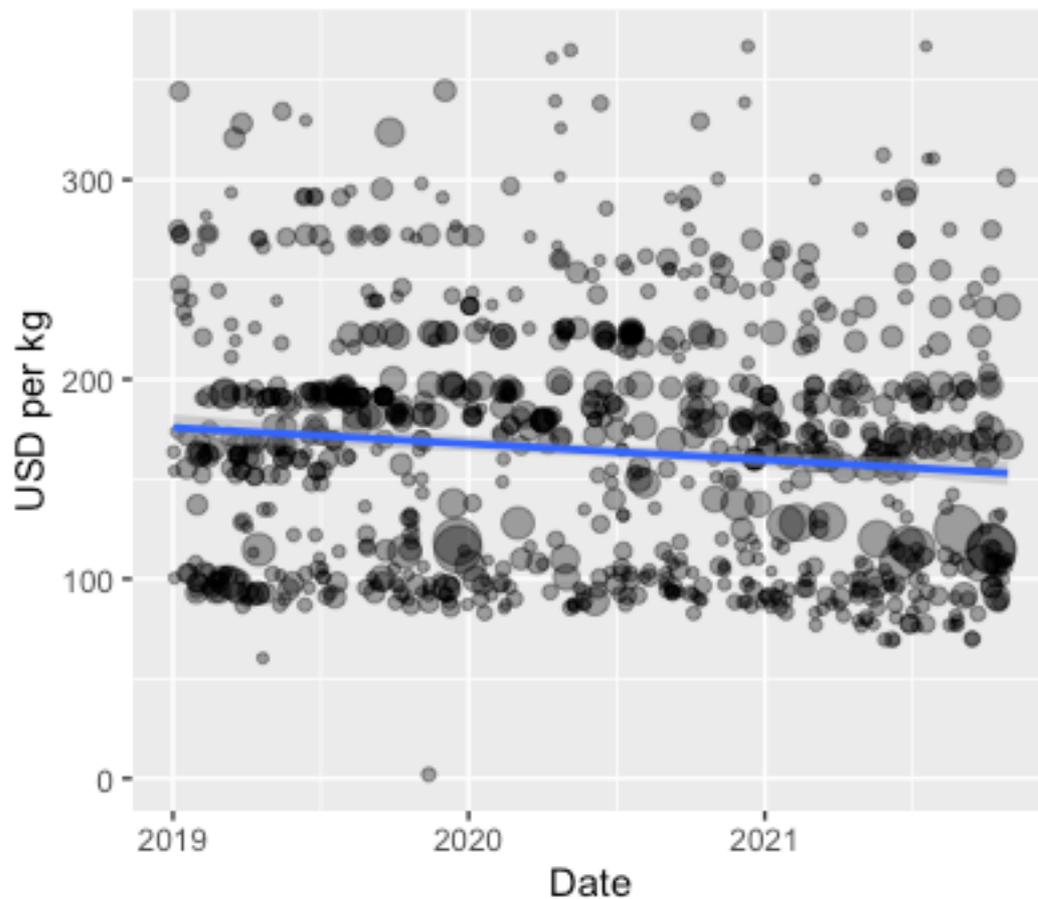


Figure 14. Telmisartan



5. API change over time visualizations: bubble charts

Bubble charts (Figures 15-18) with regional disaggregation provide a clearer visualization of the distribution in size of shipments and their destinations, as well as change over time. Each bubble represents a single shipment; the size of the bubble corresponds to the size of the shipment (kg, see legend).

Figure 15. Amlodipine bubble chart

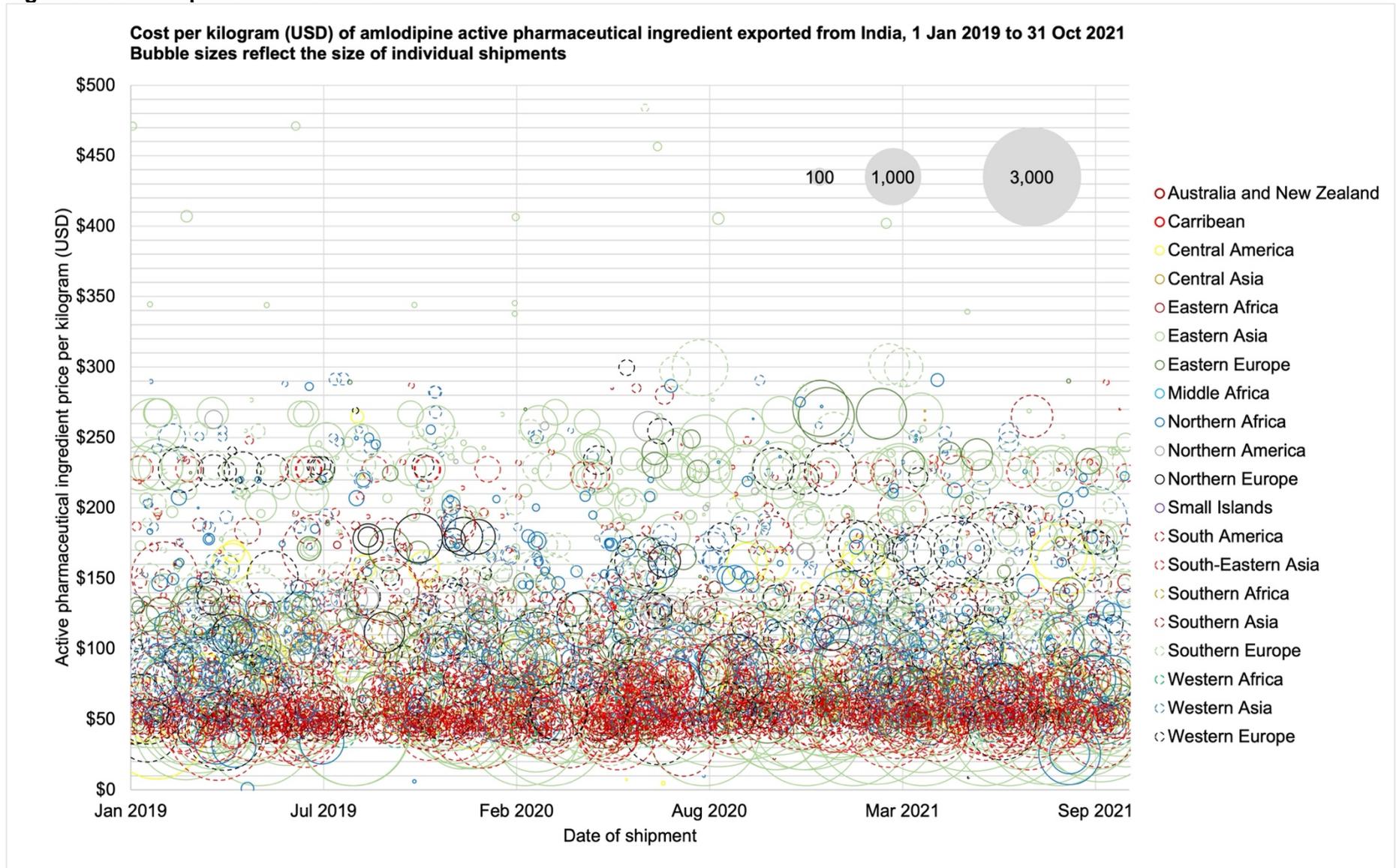


Figure 16. HCTZ bubble chart

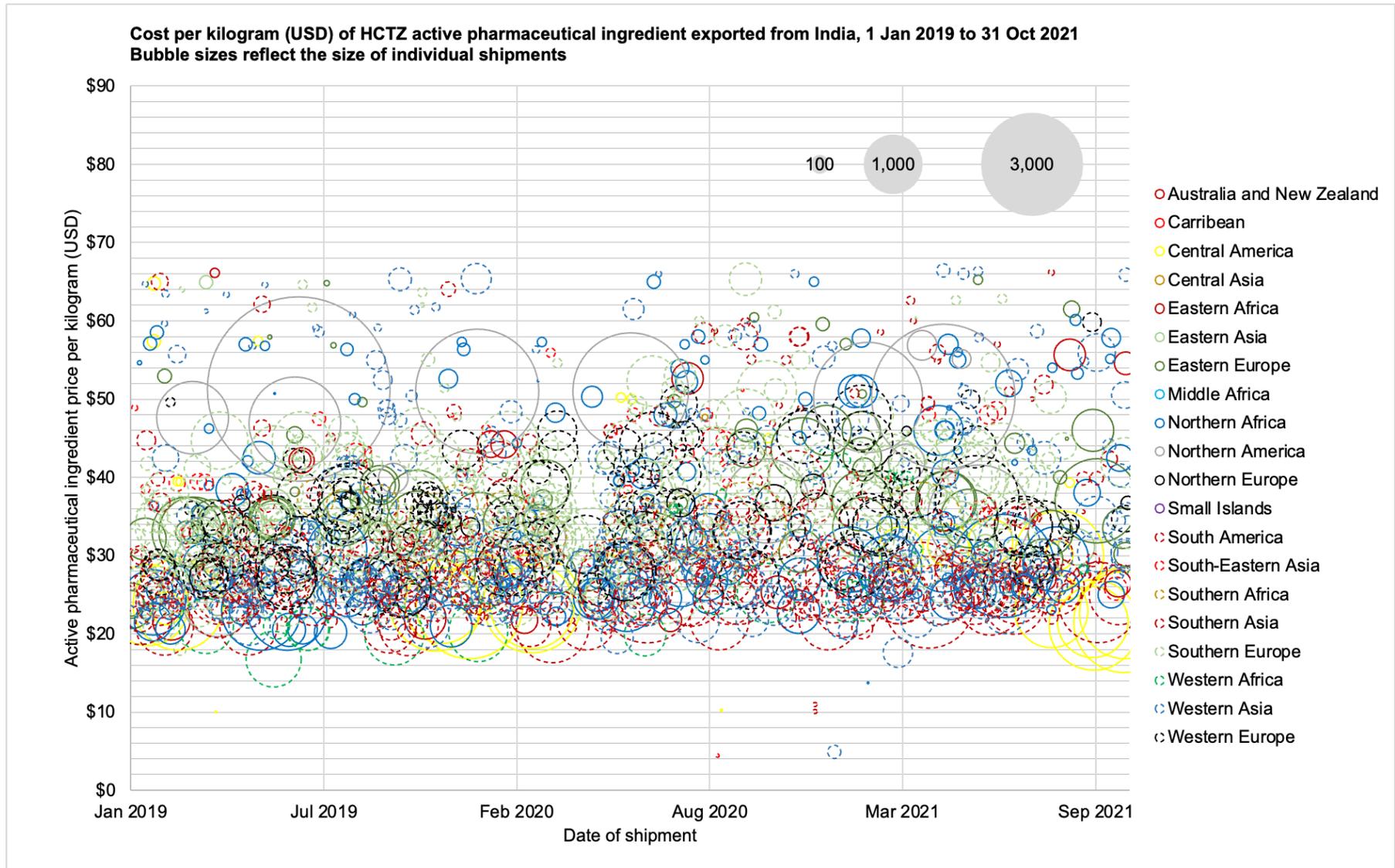


Figure 17. Losartan bubble chart

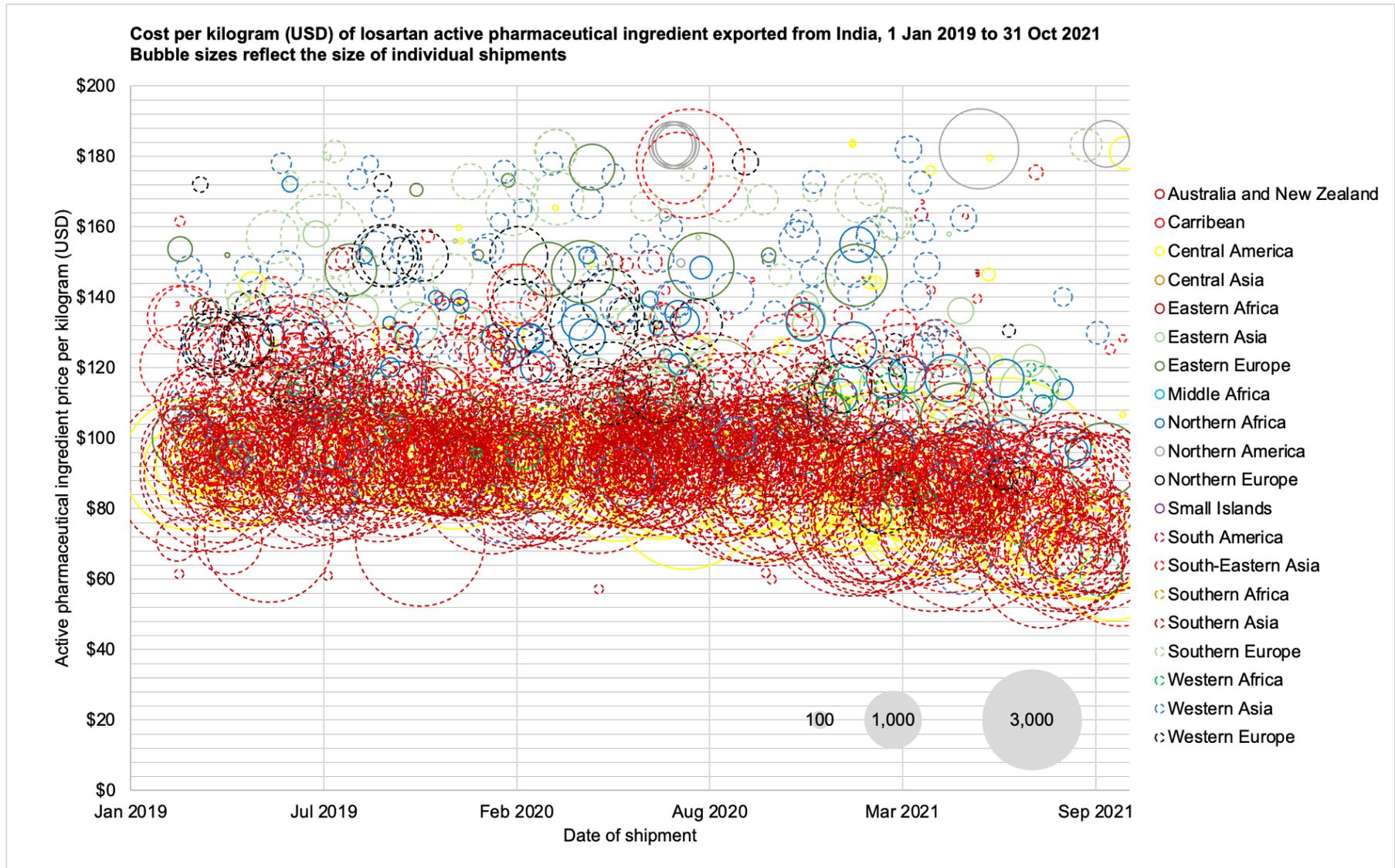
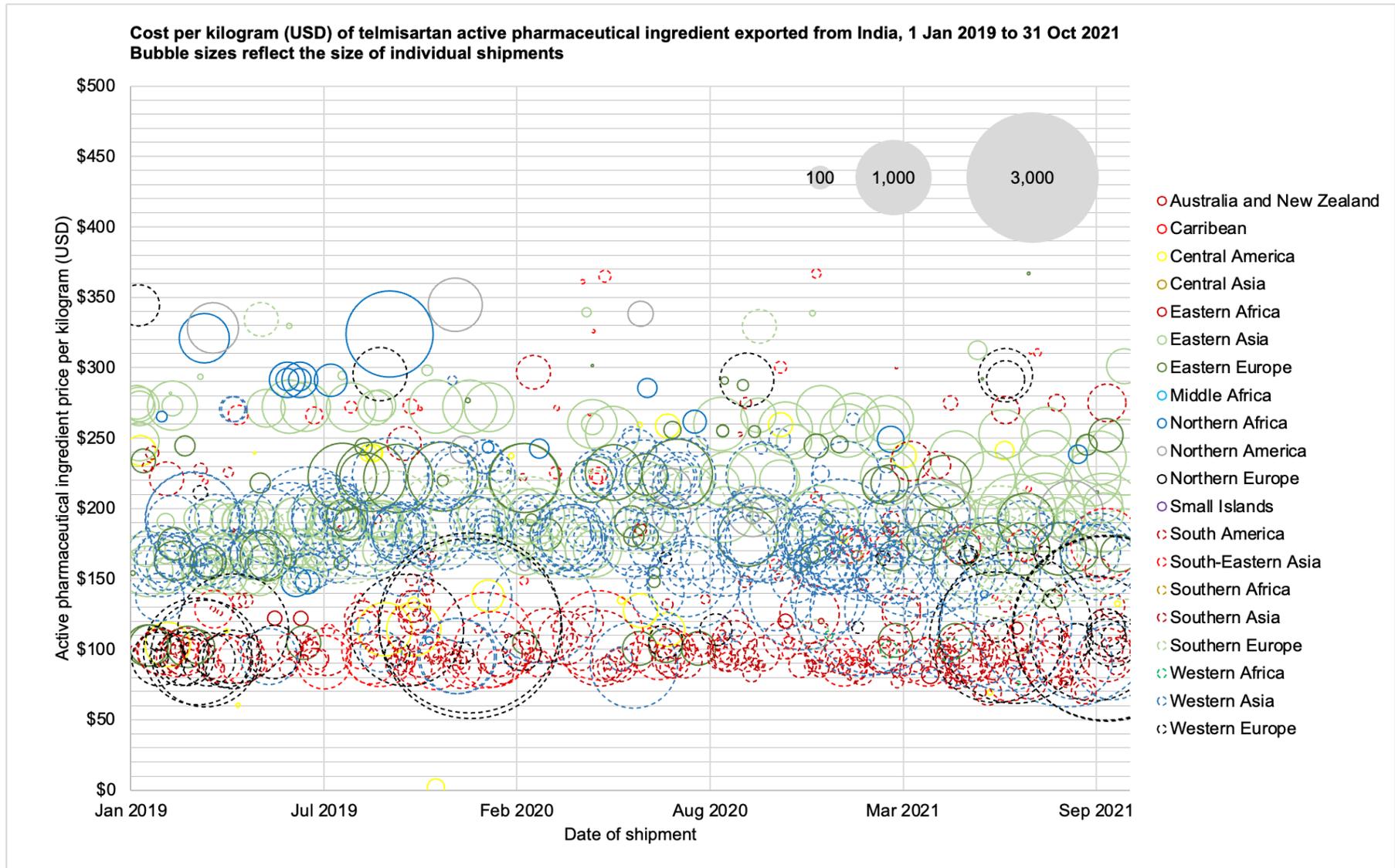


Figure 18. Telmisartan bubble chart



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- ⁱ Hill AM, Barber MJ, Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Global Health* 2018; **3**: e000571.
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Rockwood N, Cerrone M, Barber M, Hill AM, Pozniak AL. Global access of rifabutin for the treatment of tuberculosis—why should we prioritize this?. *Journal of the International AIDS Society*. 2019 Jul;22(7):e25333.
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