Short report: Cost-effectiveness of dapivirine ring compared to oral PrEP

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Declaration of Interest: LJ (Health Economics and Epidemiology Research Office (HE^{2}RO), University of Witwatersrand) has no interests pertaining to dapivirine vaginal ring.

SUMMARY

Summary Table. Cost-effectiveness comparison of dapivirine ring (DVR) vs standard of care (oral PrEP)

	Dapivirine ring analysis		
	Oral PrEP	Dapivirine ring	
		29% effectiveness	*62% effectiveness*
Incremental cost per HIV infection averted (2023-2042)			
USD	$13,445	$60,707	$26,549
ZAR	R196,393	R886,741	R387,800
Incremental cost per life year saved (2023-2042)			
USD	$4,741	$19,985	$9,337
ZAR	R69,250	R291,912	R136,378
Budget impact (2023-2027)			
Number on intervention per year	529,000-577,069	528,000-575,000	528,000-575,000
Cost per year, ZAR	R565-616 million	R999-1,088 million	R1,001-1,091 million
Threshold price for DVR to be as cost-effective as oral PrEP, ZAR			
	-	R52	R107

Modelling assumptions:
- Baseline: no PrEP
- Effectiveness: 65% (oral PrEP); 29%-62% (DVR)
- Average duration on PrEP: 5 months (oral PrEP); 5 months (DVR)
- Populations targeted: women aged 15-49, female sex workers
- Coverage: 5% across target population

Cost assumptions:
- Provision of dapivirine ring, total cost = R1,892 (incl cost of ring $14.59/R213.11 per ring)
- Provision of oral PrEP, total cost = R1,067 (incl cost of TDF/FTC R68.65/month)
- 3-monthly visits for both oral PrEP and dapivirine ring

Oral PrEP is a more cost-effective intervention in comparison to the dapivirine ring owing to the higher effectiveness and lower cost. Current price estimate for the dapivirine ring to enter the South African market is set at $14.59/ring, or R213.11/ring. For DVR to be as cost-effective as oral PrEP, it would need to cost substantially less at R52/ring (under a 29% effectiveness assumption) up to R107/ring (under a 62% effectiveness assumption).

FULL REPORT

Methods

- ***Modelling and assumptions***

The impact of PrEP (oral PrEP, dapivirine ring) on the HIV epidemic was estimated using the Thembisa model (version 4.4), a deterministic compartmental HIV transmission model of the South African HIV epidemic (Johnson and Dorrington 2021).

Oral PrEP effectiveness, accounting for both efficacy and adherence, was assumed to be 65% for women (Fonner et al. 2016). *Dapivirine ring effectiveness* was assumed to be 29% based on the pooled results from two phase III placebo-controlled randomized trials, ASPIRE and the ring study (Baeten et al. 2016; Nel et al. 2016). A second scenario was included to model an effectiveness estimate of 62%, the upper limit estimate from two open-label extension projects (OLEs), HOPE and DREAM (Baeten et al. 2021; Nel et al. 2021).

- ***Costs***

Costs were estimated from the provider perspective, the South African government. All costs are presented in both 2021 South African Rand (ZAR) and United States Dollar (USD), and uninflated. In addition, we present the numbers of women on dapivirine ring and the total cost for the next 5 years to inform the health budget.

An ingredients-based approach was used to estimate the average cost of oral PrEP (TDF/FTC) and dapivirine ring provision, using data from PrEP demonstration sites and subsequent implementation programmes, as well as following current PrEP guidelines. Full methodology for the estimation of oral PrEP cost has been described elsewhere (Jamieson et al. 2020). The cost of dapivirine ring provision was structured using similar methodology; however, we adjusted the ingredients to include the dapivirine ring, additional professional nurse time for the initial insertion of the ring at initiation, and removed laboratory monitoring tests which are not required (e.g. ALT, creatinine testing, which are included in the oral PrEP costs).

In line with standard of care PrEP, visits are scheduled 3-monthly under both the oral PrEP and dapivirine ring scenarios.

The cost of oral PrEP is set at $4.70/month (R68.65/month, based on a tender price; Master Procurement Circular January 2021; using the average 2021 exchange rate of 14.61 ZAR = 1 USD). *The cost of one dapivirine ring* (for a month) is set at $14.59/ring, or R213.11/ring (IPM price, as per NEMLC review).

- ***Scenarios***

We modelled the provision of PrEP to women aged 15-49 years, including to female sex workers, scaling up coverage to 5% across target populations for both interventions (oral PrEP, dapivirine ring). Based on data from the South African PrEP implementation programme, the average duration on oral PrEP is estimated to be 5 months (Johnson and Dorrington 2021). We assumed the same duration for women initiating on the dapivirine ring, as a best guess as no implementation data outside of a trial setting is available.

We estimated cost-effectiveness as cost per HIV infection averted and cost per life year saved over a 5- and 20-year time horizon (2023-2027 and 2023-2042), over a *baseline of no PrEP*, but including currently available HIV interventions in South Africa (e.g. high coverages for condom provision, HIV testing services, and medical male circumcision). This allows us to determine the impact of a reduction in HIV incidence due to oral PrEP and the dapivirine ring on the need for subsequent ART, in addition to existing prevention interventions. The estimation of the cost of the HIV programme followed the same methodology as the South African HIV Investment Case.

- ***Threshold* analysis**

Anticipating a lower cost-effectiveness of the dapivirine ring due to a higher cost of the ring, and lower effectiveness, compared to oral PrEP, we conduct a threshold analysis on the price to estimate the price level at which the dapivirine ring is similarly cost-effective compared to oral PrEP.

Results

Table 1. Estimated cost of dapivirine and ring oral PrEP provision, per person initiated

	Dapivirine ring			Oral PrEP		
	Cost (USD)	***Cost (ZAR)***	***%***	***Cost (USD)***	***Cost (ZAR)***	***%***
Drugs	88	1,279	68%	28	412	37%
Labs	7	98	5%	16	235	21%
Consumables	0.5	7	0.3%	1	21	3%
Staff	27	394	21%	19	280	29%
Overheads	8	114	6%	8	120	11%
Total Cost	**130**	**1,892**		**73**	**1,067**	

The cost of provision of dapivirine ring and oral PrEP was estimated at $130 and $73 per woman initiated, respectively, for the average duration of 5 months after initiation, that they are in the PrEP programme (Table 1).

Table 2a. Impact and cost-effectiveness of dapivirine ring and oral PrEP over a 5- and 20-year time horizon (2021 USD)

		Dapivirine ring		
	Baseline	*29% effectiveness*	*62% effectiveness*	Oral PrEP
5-year time horizon (2023-2027)				
Total Cost of the HIV programme (USD, billions)	10.04	10.40	10.39	10.24
Incremental cost (USD, billions)	-	352 (4%)	350 (3%)	195 (2%)
Total new HIV infections (thousands)	0.91	0.91	0.90	0.90
HIV infections averted (thousands)	-	5.5 (1%)	13.6 (1%)	14.3 (2%)
Total life years lost to AIDS (millions)	11.39	11.39	11.39	11.39
Life years saved (thousands)	-	0.5 (0.004%)	6 (0.1%)	7 (0.1%)
Incremental cost per HIV infection averted (USD)	**-**	***63,477***	***25,859***	***13,637***
Incremental cost per life year saved (USD)	**-**	***693,612***	***58,204***	***29,853***
20-year time horizon (2023-2042)				
Total Cost of the HIV programme (USD, billions)	41.40	43.05	43.00	42.25
Incremental cost (USD, billions)	-	1,650 (4%)	1,598 (4%)	850 (2%)
Total new HIV infections (millions)	2.94	2.91	2.88	2.88
HIV infections averted (thousands)	-	27 (1%)	60 (2%)	63 (2%)
Total life years lost to AIDS (millions)	36.02	35.94	35.85	35.84
Life years saved (thousands)	-	83 (0.2%)	171 (0.5%)	179 (0.5%)
Incremental cost per HIV infection averted (USD)	**-**	***60,707***	***26,549***	***13,445***
Incremental cost per life year saved (USD)	**-**	***19,985***	***9,337***	***4,741***

Table 2b. Impact and cost-effectiveness of dapivirine ring and oral PrEP over a 5- and 20-year time horizon (2021 ZAR)

		Dapivirine ring		
	Baseline	*29% effectiveness*	*62% effectiveness*	Oral PrEP
5-year time horizon (2023-2027)				
Total Cost of the HIV programme (ZAR, billions)	146.71	151.85	151.83	149.56
Incremental cost (ZAR, billions)	-	5.1 (4%)	5.1 (3%)	2.8 (2%)
Total new HIV infections (thousands)	0.91	0.91	0.90	0.90
HIV infections averted (thousands)	-	5.5 (1%)	13.6 (1%)	14.3 (2%)
Total life years lost to AIDS (millions)	11.39	11.39	11.39	11.39
Life years saved (thousands)	-	0.5 (0.004%)	6 (0.1%)	7 (0.1%)
Incremental cost per HIV infection averted (ZAR)	**-**	***927,197***	***377,720***	***199,193***
Incremental cost per life year saved (ZAR)	**-**	***10,131,497***	***850,183***	***436,056***
20-year time horizon (2023-2042)				
Total Cost of the HIV programme (ZAR, billions)	604.68	628.79	628.03	617.10
Incremental cost (ZAR, billions)	-	24.1 (4%)	23.3 (4%)	12.4 (2%)
Total new HIV infections (millions)	2.94	2.91	2.88	2.88
HIV infections averted (thousands)	-	27 (1%)	60 (2%)	63 (2%)
Total life years lost to AIDS (millions)	36.02	35.94	35.85	35.84
Life years saved (thousands)	-	83 (0.2%)	171 (0.5%)	179 (0.5%)
Incremental cost per HIV infection averted (ZAR)	**-**	***886,741***	***387,800***	***196,393***
Incremental cost per life year saved (ZAR)	**-**	***291,912***	***136,378***	***69,250***

Over a 20-year time horizon, oral PrEP is estimated to be more cost effective, at $13,445/HIV infection averted, compared to the dapivirine ring under both 29% effectiveness ($60,707/HIV infection averted) and 62% effectiveness ($26,549/HIV infection averted) (Table 2a). Similar conclusions are reached under the 5-year time horizon analysis, and for incremental cost per life year saved. Note, the incremental cost per life year saved is substantially higher in the 5-year time horizon analysis as the effects of AIDS deaths have not yet been realized in the short time frame.

Results in ZAR are shown in Table 2b.

Table 3. Cost estimates for budget, years 2022/23 to 2026/27

	2022/23	2023/24	2024/25	2025/26	2026/27
Number of dapivirine ring clients	528,259	535,369	547,638	561,056	575,189
Total cost of dapivirine ring (USD, millions)	68	69	71	73	75
Total cost of dapivirine ring (ZAR, millions)	999	1,013	1,036	1,061	1,088

Assuming a coverage rate of 5% for 15-49-year-old women, we can expect a total of 528,000 to 575,000 women to take up the dapivirine ring at a cost of R999-R,1088 million (or $68-75 million) per year, over the next 5 years and assuming the cost of the ring remains at $14.59 or R213.11 per ring and women remain on the dapivirine ring for an average of 5 months.

Table 4. Threshold analysis: estimated price at which the dapivirine ring remains as cost-effective as oral PrEP

Solving for		***29% effectiveness***	***62% effectiveness***
Incremental cost/HIV infection averted			
	USD	$3.33	$7.33
	ZAR	R49	R107
Incremental cost/life year saved			
	USD	$3.54	$7.35
	ZAR	R52	R107

The estimated price at which the dapivirine ring becomes similarly cost-effective compared to oral PrEP would be $3.54/ring (if assuming 29% effectiveness) and ~$7.35/ring (if assuming 62% effectiveness).

Conclusion

Assuming the same duration and coverage between the PrEP interventions and the same target population, oral PrEP is more cost-effective than the dapivirine ring. This is mostly due to both the higher effectiveness (65% for oral PrEP vs 29% for dapivirine ring) and the lower cost per month of provision ($73 or R1,067 per woman initiated for oral PrEP vs $130 or R1,892 per woman initiated for dapivirine ring).

If the dapivirine ring achieves a consistent 62% effectiveness, it will still be less cost-effective compared to oral PrEP, as long as the price remains higher than $7.35/ring. A lower effectiveness of the dapivirine ring will result in the lower price per ring required in order to meet the same level of cost-effectiveness compared to oral PrEP.

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