COVID-19 Oral Antivirals in Africa: Unlocking Value and Potential

Are investments in oral antivirals cost-effective for Africa?

POLICY BRIEF September 2023

This Policy Brief builds on a growing body of evidence generated through the Africa CDC's Health Economics and Financing Programme (HEP) to support and accelerate informed decision-making and policy responses across the African continent. This brief summarizes the latest evidence on the potential role and value-for-money of COVID-19 Oral Antivirals (COAVs), and helps to answer the following policy question: **are investments in COAVs cost-effective for African countries?**

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KEY MESSAGES

1 Both Paxlovid and Molnupiravir are cost-effective in high-risk unvaccinated patients in all three national-contexts, although this was significantly influenced by various factors such as early treatment initiation and hospitalization rates.

2 Paxlovid generally achieved a higher Incremental Net Monetary Benefit (NMB) than Molnupiravir, suggesting more value can be achieved for the additional cost. However, this finding should be interpreted cautiously due to the absence of direct head-to-head comparison trials.

3 Under certain scenarios, including a 100% likelihood of early treatment initiation, both COAVs dominated (i.e. were less costly and more effective) usual care in all target populations, except for Molnupiravir for the all-adult population in Rwanda.

4 This evidence broadly affirms the decisions of African governments to avoid substantial procurement of either COAV. However, it suggests that Paxlovid might offer good value for money when targeting specific populations

5 While this evidence is based on three countries, by explicitly modeling the nuances and diversities in key parameters relevant to the African setting, the study provides useful insights to policymakers on a range of context-specific factors that should be considered when making funding and allocation decisions on COAVs based on findings from cost-effectiveness analyses.

6 The cost-effectiveness of both COAVs is significantly impacted by their cost, suggesting that access to these treatments at lower prices is crucial for their cost-effectiveness and economic viability in Africa.

7 The findings underscore the importance of early treatment initiation for cost-effectiveness of both COAVs. Investments in measures that enhance early detection and treatment are likely to improve COAV cost-effectiveness.

OBJECTIVES

This Policy Brief summarizes findings from model-based cost-effectiveness analyses, in which the costs and health outcomes arising from early treatment initiation for two alternative COVID-19 Oral Antivirals (COAVs), Paxlovid (Nirmatrelvir/Ritonavir) and Molnupiravir (Lagevrio), were individually compared to usual care (without COAVs). These COAVs were among the first to be authorized to prevent severe illness progression in high-risk populations with mild to moderate COVID-19.

The study focused its analyses on three target unvaccinated populations in Ghana, Rwanda, and Zambia. With the continent characterized by a wide range in population vaccine coverage rates and testing capacities for COVID-19, the purposeful selection of these national contexts facilitates explicit consideration of nuances relevant to the African setting.

The objective is to support policymakers on decisions regarding the allocation of scarce resources for COVID-19 management, providing valuable insights on the conditions under which COAVs can achieve the greatest benefits and optimize the allocation of finite resources

BACKGROUND

African Union (AU) Member States (MS) have initiated strategic responses to support health and economic recovery and advance regional health system security. As the continent transitions from emergency response to integrated, routine management of COVID-19, severe long- and short-term COVID-19 infections remain an ongoing concern, especially for groups at higher risk, including those with underlying conditions that weaken immune response, and unvaccinated populations.

Inpatient hospital care needs for severe COVID-19 disease impose substantial costs, exacerbate health system pressures, and redirect vital resources from the prevention and control of existing high-burden diseases, and broader unmet population health needs. These realities risk undermining continental aspirations, especially given the unknown evolution of the virus and prevailing vaccination coverage rates across the continent.

Therefore, COVID-19 priorities have since reoriented toward preventing severe disease progression. The Test-to-Treat Initiative launched by the Africa CDC is purposefully intended to reduce health system surges and avert avoidable hospitalizations due to severe COVID-19 across high-risk groups. The emergence of COVID-19 oral antiviral treatments (COAVs) therefore presents a potential turning point in managing the pandemic, provided they are cost-effective and accessible.

Both Paxlovid (Nirmatrelvir/Ritonavir) and Molnupiravir (Lagevrio), were among the first COAVs to be authorized for use and are endorsed by the Africa CDC. These treatments work by inhibiting the replication of the SARS-CoV-2

COAVs have been proven to reduce hospitalizations and deaths in unvaccinated and high-risk groups. Various initiatives and voluntary licensing agreements have laid a foundation for access to affordable generic COAVs on the continent.

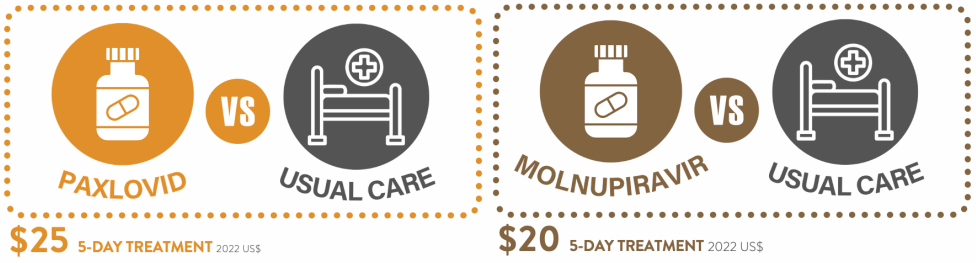
However, the extent of their benefit is tied to factors such as cost, accessibility, and timing of initiation relative to infection. Further, their effectiveness and value-for-money in African contexts remains unknown and cannot be directly inferred from their use in high-income contexts. Variation in the burden of disease, the state of health systems, and probability of early treatment initiation are factors likely to influence these outcomes, particularly in settings compromised by limited testing capacity.

APPROACH

In the primary study, decision-tree modelling simulated mild-to-moderate COVID-19 disease progression arising under the administration of Paxlovid and Molnupiravir for three specific unvaccinated populations: (1) patients aged 65 years and above (elderly); (2) adult patients with at least one other underlying risk factors for disease severity; and (3) all unvaccinated adult patients. Integrating local epidemiological and demographic parameters to capture transmission dynamics and population characteristics, disease progression and overall health outcomes were estimated for each hypothetical population cohort, compared with usual care over a 30-day period (acute COVID-19 disease).

Costs associated with outpatient and inpatient clinical management as well as the full 5-day treatment course for each COAV were estimated from a public payer's perspective. Overall health benefits were valued in terms of disability adjusted life-years (DALYs). To enable a comparative assessment of each COAV against usual care, value for money was reported in terms of incremental cost-effectiveness ratios (ICERs), measured as the cost per DALY averted, as well as Net Monetary Benefits (NMB). Cost-effectiveness was determined using country-specific marginal productivity of health systems estimates as thresholds of value for money (Ghana, USD 433.25; Rwanda, USD 246.50; Zambia, USD 503.50). All costs are expressed in 2022 US dollars.

COSTS AND OUTCOMES ARISING FROM EARLY TREATMENT INITIATION VIA ADMINISTRATION OF PAXLOVID (NIRMATRELVIR/RITONAVIR) AND MOLNUPIRAVIR (LAGEVRIO) WERE INDIVIDUALLY COMPARED TO USUAL CARE (WITHOUT COAVs) USING DECISION-TREE MODELLING .



PAXLOVID AND MOLNUPIRAVIR ARE BOTH TAKEN BY MOUTH TWICE DAILY FOR 5 DAYS.

THE STUDY FOCUSED ITS ANALYSES ON THREE TARGET UNVACCINATED POPULATIONS PRESENTING SYMPTOMS CONSISTENT WITH MILD-TO-MODERATE COVID-19

EXPLICIT CONSIDERATION OF VACCINATION COVERAGE AND THE PROBABILITY OF EARLY TREATMENT INITIATION WAS ENABLED BY TAILORING MODEL PARAMETERS TO THE NATIONAL CONTEXTS OF GHANA, RWANDA AND ZAMBIA.

	PROBABILITY OF EARLY TREATMENT INITIATION COVID-19 tests performed/1000 population	COVID-19 VACCINE COVERAGE Population (%) vaccinated against COVID-19
GHANA	LOW 0-100	FAIR 27%
ZAMBIA	FAIR 100-200	LOW 12%
RWANDA	HIGH 200-1000	HIGH 65%

For in-depth methodological and model parameter details, please refer to the published preprint of the original study

CLICK OR SCAN TO ACCESS THE PREPRINT OF THE ORIGINAL STUDY

KEY FINDINGS

The study found both Paxlovid and Molnupiravir could be cost-effective for high-risk unvaccinated patients. However, these results were sensitive to key parameters like the likelihood of early treatment initiation and hospitalization rates. Across all countries, the provision of Molnupiravir and Paxlovid to the adult population presenting with mild-to-moderate COVID-19, without specifically targeting high-risk and unvaccinated individuals, is unlikely to be a cost-effective alternative to usual care.

The findings varied across the three countries and target populations. In elderly patients, Paxlovid was less costly and more effective (i.e., dominated) than standard of care in all three study countries. Molnupiravir dominated standard of care in Rwanda and Zambia and an incremental cost-effectiveness ratio (ICER) was estimated at US$1023.58 per disability-adjusted life year (DALY) averted in Ghana. In adults with other underlying risk factors, Paxlovid dominated in Rwanda and Zambia while Molnupiravir dominated in Rwanda.

- **Neither Paxlovid nor Molnupiravir were cost-effective in the all-adult group in any country context.**
- **In elderly patients, Paxlovid was less costly and more effective (i.e. dominated) than usual care in all three study countries.**
- **Molnupiravir dominated usual care in Rwanda and Zambia and an incremental cost-effectiveness ratio (ICER) was estimated at US$1024 per disability-adjusted life year (DALY) averted in Ghana.**
- **In adults with other underlying risk factors, Paxlovid dominated in Rwanda and Zambia while Molnupiravir dominated in Rwanda.**

Using country-specific marginal productivity of health systems estimates as thresholds of value for money: Ghana: USD 433.25 (2022); Rwanda: USD 246.50 (2022); Zambia: USD 503.50 (2022)

ICER'S FOR BASE CASE SCENARIO

	GHANA	RWANDA	ZAMBIA
ALL ADULTS			
PAXLOVID VS USUAL CARE	$ 26 107.26	$ 2 302.22	$ 6 944.05
MOLNUPIRAVIR VS USUAL CARE	$ 78 165.74	$ 11 999.66	$ 24 614.18
ELDERLY >=65 YEARS			
PAXLOVID VS USUAL CARE	$ -3 030.31	$ -4 011.16	$ -3 611.13
MOLNUPIRAVIR VS USUAL CARE	$ 1 023.58	$ -3 913.69	$ -2 839.08
ADULTS WITH OTHER RISK FACTORS			
PAXLOVID VS USUAL CARE	$ 4 259.82	$ -2 519.90	$ -877.04
MOLNUPIRAVIR VS USUAL CARE	$ 20 307.18	$ -20.22	$ 4 099.06

Note: Negative ICERs show cost saving compared to usual care

The significant role of vaccination status in determining cost-effectiveness was highlighted by the findings; scenarios modelling the initiation of COAVs to vaccinated adult patients were not found to yield cost-savings or net health benefits. Paxlovid was however cost-effective for vaccinated elderly patients in Zambia and Rwanda but not in Ghana.

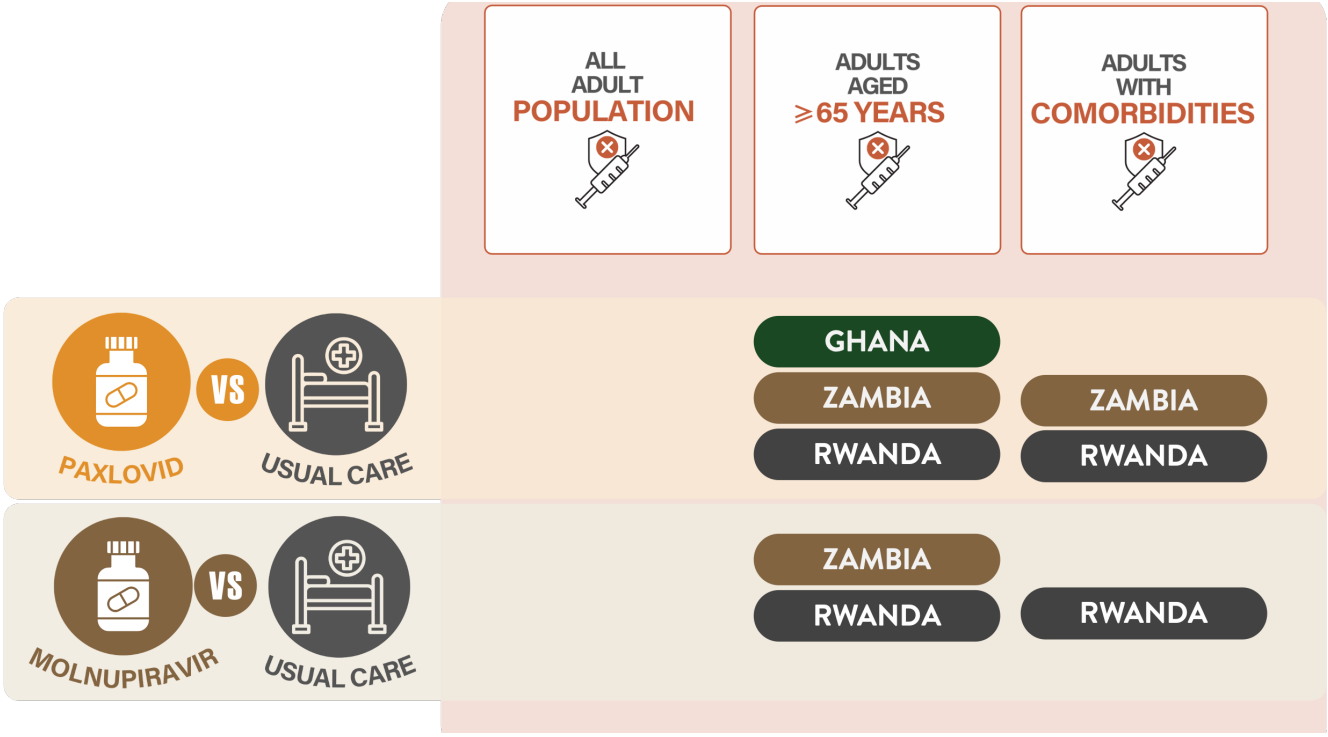
The most influential parameters on cost-effectiveness for both Paxlovid and Molnupiravir, compared to usual care were:

- **COAV treatment costs**
- **Likelihood of initiating treatment within five days of symptom onset**
- **Hospitalization rates for elderly and high-risk unvaccinated populations**

For Molnupiravir (only) treatment effect was also found to be a significant determinant of cost-effectiveness.

The timely initiation of treatment, specifically within the first 5 days of symptom onset, was identified as a critical factor for achieving cost-effectiveness. Notably, in the Rwandan context, Molnupiravir was determined to be cost-effective, but this was largely confined to unvaccinated, high-risk adult populations, presumably due to the greater emphasis on early treatment initiation in this setting.

Paxlovid generally had a higher Incremental Net Monetary Benefit (NMB) than Molnupiravir, indicating more value per additional cost. Nonetheless, direct comparisons are limited by differences in their randomized controlled trial (RCT) conditions.



IMPLICATIONS FOR COUNTRIES

1 Recognize the importance of early treatment initiation.

The effectiveness and cost-effectiveness of both Paxlovid and Molnupiravir rely heavily on the likelihood of early treatment initiation (within 5-days of symptom onset). Policy priorities should emphasize timely detection and treatment for COVID-19 disease.

2 Secure lower prices

Given the significant impact of treatment cost on cost-effectiveness, affordable pricing of COAVs is fundamental to their economic viability. At treatment costs similar to high income countries, Paxlovid (approximately $600 per 5-day course, vs 2022 US $25 modelled in this study) and Molnupiravir (approximately $700 per 5-day course vs 2022 US $20 modelled in this study) will not be cost-effective for any target population, irrespective of early treatment initiation and risk.

3 Focus on high-risk populations

As both Paxlovid and Molnupiravir showed cost-effectiveness in high-risk, unvaccinated populations, targeted treatment strategies and patient prioritization could be considered, particularly for elderly adults.

4 Monitor and adjust for emerging evidence

As new evidence from randomized controlled trials emerges, cost-effectiveness should be reassessed. Additionally, head-to-head comparison trials between Paxlovid and Molnupiravir would provide a more definitive perspective on their relative cost-effectiveness.

5 Contextualize findings to local settings

Given the variability in key parameters across different settings, findings from cost-effectiveness analyses should be carefully contextualized for local decision-making processes.

ABOUT THE STUDY

The Africa CDC Health Economics and Financing Programme and Center for Global Development oversaw the analyses informing this brief. The study was funded by the Bill and Melinda Gates Foundation as part of the International Decision Support Initiative (IDSI).