

# Dolutegravir and sexual dysfunction

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## Introduction

Dolutegravir-based antiretroviral regimens for the treatment of HIV have reported high levels of effectiveness and acceptability<sup>1</sup>. It is now a recommended first- or second-line HIV treatment, with the potential to reach 38 million patients worldwide, but concerns have been raised about potential side effects, including sexual dysfunction<sup>2</sup>. However, sexual dysfunction in HIV-infected people can be multifactorial with organic and psychological components<sup>3</sup> and the potential role of other HIV treatments in sexual dysfunction has also been discussed<sup>4</sup>.

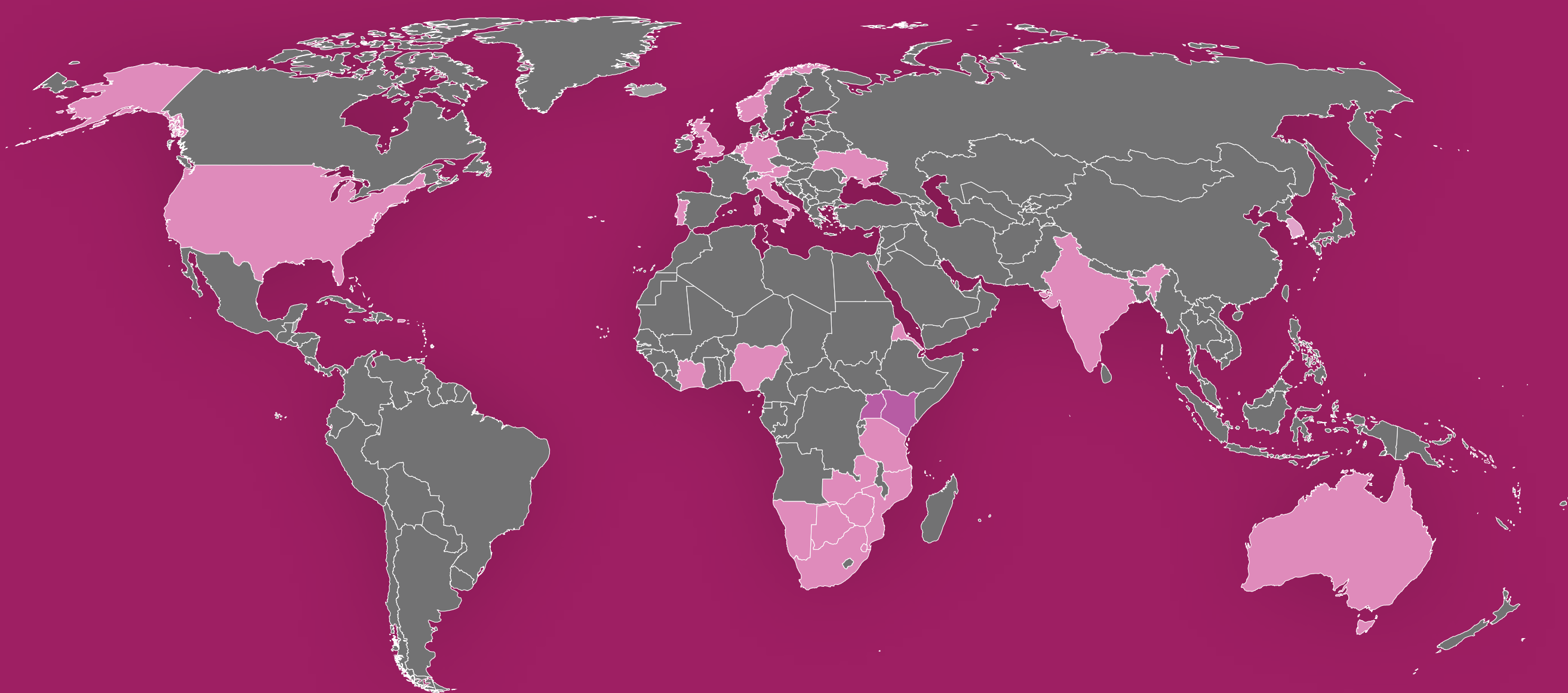


Figure 1. Countries with reports for dolutegravir and sexual dysfunction (SMQ)

## Methods

A search of VigiBase, the WHO global database of individual case safety reports, was performed on 11 April 2023. Cases were identified when they reported both a reaction in the Standardised MedDRA Query (SMQ) "Sexual dysfunction (narrow)" and dolutegravir-containing products in the WHODrug Standardised Drug Grouping (SDG) "Drugs for treatment of HIV infections". Disproportionality measures, using the information component values, were calculated for the combination of the SMQ and dolutegravir-containing products. An  $IC_{025}$  of greater than 0 indicates positive disproportionate reporting with statistical significance<sup>5</sup>. *vigiPoint*<sup>6</sup> was used to compare reporting for medications containing dolutegravir with medications that do not contain dolutegravir in the WHODrug SDG "Drugs for treatment of HIV infections". The positive lower end of the 99% credibility interval for the calculated shrinkage log odds ratio (SLOR) highlights variables with an over-representation among the dolutegravir subset. A threshold of greater than 0.5 for the lower end of the 99% credibility interval ( $SLOR_{005}$ ) highlights substantial deviation.

Table 1. *vigiPoint* results for MedDRA High Level Group Terms and High Level Terms related to sexual dysfunction when comparing dolutegravir-containing HIV treatment to non-dolutegravir containing HIV treatments. Total case count for DTG: 26,589; for all anti-HIV excluding DTG: 321,610. Abbreviations: DTG – dolutegravir; SLOR – Shrinkage Log Odds Ratio;  $SLOR_{005}$  refers to the lower end of the 99% credibility interval.

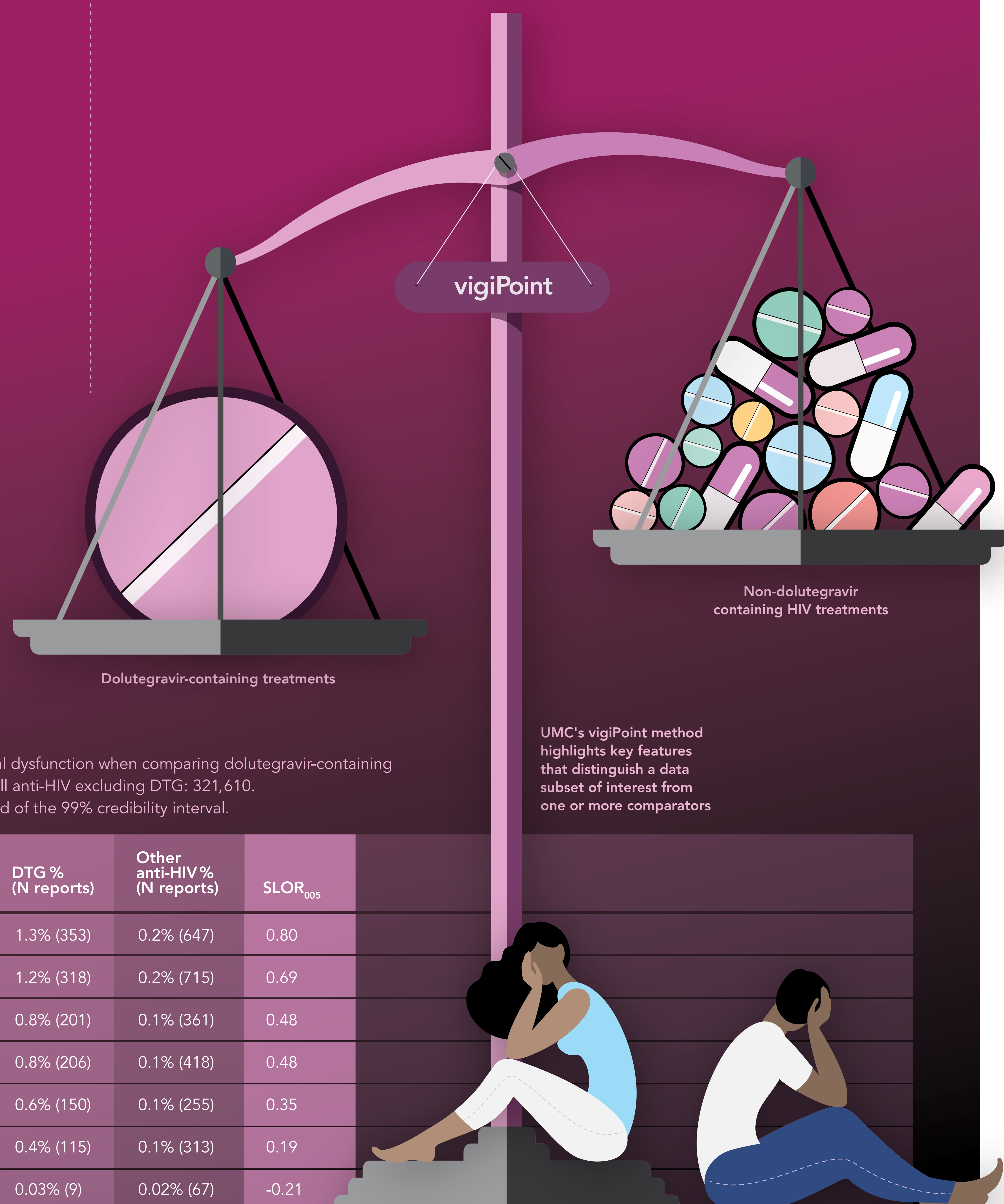
MedDRA level	Term	DTG % (N reports)	Other anti-HIV % (N reports)	$SLOR_{005}$
High Level Group Term	Sexual dysfunctions, disturbances and gender identity disorders	1.3% (353)	0.2% (647)	0.80
High Level Group Term	Sexual function and fertility disorders	1.2% (318)	0.2% (715)	0.69
High Level Term	Sexual arousal disorders	0.8% (201)	0.1% (361)	0.48
High Level Term	Erection and ejaculation conditions and disorders	0.8% (206)	0.1% (418)	0.48
High Level Term	Sexual desire disorders	0.6% (150)	0.1% (255)	0.35
High Level Term	Sexual function and fertility disorders NEC	0.4% (115)	0.1% (313)	0.19
High Level Term	Sexual dysfunction NEC	0.03% (9)	0.02% (67)	-0.21

## Results

For all dolutegravir-containing active ingredients, a total of 348 reports were identified in VigiBase. The countries that contributed the largest number of reports were Uganda (n=147, 42.2%) and Kenya (n=81, 23.3%) with reports received from 28 countries (see Figure 1), the WHO regions represented being AFR, AMR, SEAR, EUR and WPR. The  $IC_{025}$  value for this combination was 2.0, indicating statistically significant disproportionate reporting for this combination. The most common reported MedDRA Preferred Terms were "Erectile dysfunction" (n=201), "Libido decreased" (n=86) and "Loss of libido" (n=48). The results of the *vigiPoint* analysis are shown in Table 1, with High Level Group Terms and High Level Terms related to sexual dysfunction.

## Conclusions

This complex potential signal warrants further investigation. The initial results are supportive but not conclusive. Case-by-case analysis and collaboration with contributing national centres are crucial next steps.



## References

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