RISK ASSESSMENT

AUTOCHTHONOUS TRANSMISSION OF MPOX CLADE IB IN THE EU

The risk assessment was published 5/11/2025 at https://www.sciensano.be/en/projects/coordination-risk-assessment-group.

RAG person of contact:
Jorgen Stassijns (+ 32 478 84 02 91 or jorgen.stassijns@sciensano.be) and rag@sciensano.be

SIGNAL	Detection of autochthonous transmission of monkeypox virus Clade Ib/sh2023 in EU/EEA

DESCRIPTION

Event

Since 10 October 2025**, four EU/EEA countries have reported locally-acquired mpox Clade Ib/sh2023 cases (no travel history or link to imported case).** This is an important change from the previously reported 30 EU/EEA mpox clade I cases which had been imported or linked to imported cases – with onward transmission limited only to household contacts (1).

The cases have been reported from Spain (1 case), Italy (2 cases), Portugal (1) and the Netherlands (1). Among these five cases, two mentioned having sex with men, one was vaccinated, and none had severe disease. Concurrently, infections with Clade Ib/sh2023 mpox without travel link have been reported in the UK in April 2025 and in the USA (California) in October 2025 (WHO Mpox Dashboard).

During 2025, a total of 59 mpox cases (clade I and II) were reported in Belgium. For those among which clade subtyping was performed, there were 5 Clade Ib/sh2023 (all imported or linked to import) and 25 clade II infections. The majority of mpox cases were men (88.9%) and between the ages of 20-50 (83.6%). Most cases were sexually transmitted (83% of those with known info). Six cases reported previous mpox two-dose vaccination (10.1%) and only one case reported previous mpox infection (1.7%).

Among the cases with information on sexual behaviour, 30 (71%) were reported as **men who have sex with men** (MSM) and 12 as heterosexual. HIV status was known for 38 of the 59 cases, among which 4 (10%) were HIV positive. Information on PrEP use was available for 41 cases, among which 15 (37%) reported using PrEP. There were 5 reported hospitalisations: 2 for isolation and 3 for supportive care.

No patient was admitted to intensive care nor died. All Clade Ib/sh2023 cases were imported and one case led to self-limited household transmission, but without introduction into sexual networks.

Type of risk: Unusual	Previous risk assessments in 2024 have signalled that, just as during the 2022 Clade IIb/sh2017 mpox pandemic, there remains a risk of importation of Clade Ib/sh2023 with either 1) subsequent (self-limiting) household outbreaks or 2) introduction into a sexual networks, including among MSM, which could lead to propagated spread through close-contact exposure across multiple contacts. So far, Clade Ib/sh2023 transmission in Europe had remained confined to household spread. This now is the **first signal of a possible introduction of mpox Clade Ib/sh2023 into sexual networks** among men who have sex with men in several EU/EEA countries.
Severity of the risk: Low	Early estimates of severity of clade I MPXV were based on observations in endemic provinces of the DRC. The CFR ranged up to 11%, giving rise to concerns about higher intrinsic severity of clade I. As noted in previous risk assessments, these estimates were affected by under-ascertainment of less severe cases and reflected the poor health and nutritional status and lack of healthcare access among the affected population, many of whom were young children. Based on the current syndromic surveillance of mpox (i.e. suspected cases) in the Democratic Republic of the Congo, **WHO reports a case fatality rate (CFR) of respectively 0.2% (95% CI 0.1% - 0.2%) and 0.1% (0.0% - 0.1%) in South Kivu and North Kivu**, two provinces where **Clade Ib/sh2023** is predominant. In Kinshasa, where clades Ia and Ib co-circulate, the reported CFR is 0.3% (0.2% - 0.4%). These estimates are very close to the mortality observed among cases due to **Clade IIb/sh2017** in Belgium, with 2 deaths among 908 cases (CFR 0.2%) since 2022. These two deaths occurred among patients with severe underlying health conditions. Generally, children, pregnant women and people with weak immune systems, including people living with HIV that is not controlled, are considered at higher risk for serious illness and death due to complications from mpox (2). Evidence specifically for Clade Ib/sh2023 is however limited but it is very likely that this risk is similar as for Clade IIb/sh2017. A systematic review on data until September 2024 on risk factors for severe disease found little information on clinical outcomes among children and pregnant women (3). A pre-print study based on data from 69 pregnant women infected with Clade I (a or b) showed that 50% of these pregnancies resulted in fetal loss or congenital mpox, indicating that mpox infection is clearly linked with vertical transmission and adverse pregnancy outcomes (link).
Exposed population	**At-risk population** The population most likely to be exposed to mpox Clade Ib/sh2023 are household or sexual contacts of mpox infected people, travellers to countries/regions with established endemic circulation and healthcare workers caring for mpox cases and not wearing appropriate PPE. Considering the transmission of the 2022 Clade IIb/sh2017 outbreak among sexual networks of MSM, and the current identification of non-travel related mpox cases that have reported sex with men in the EU/EEA, **there is a risk of circulation among sexual networks of MSM**. The risk of exposure increases with the number of sexual partners. Not taking into account immunity status, we estimate that one of the highest-risk populations of MSM with multiple sexual partners concerns approximately **10.100** individuals (number of registered **PrEP** users in 2024). The higher risk in this population is confirmed by the high proportion (37%) of PrEP users among mpox cases in Belgium in 2025. This number is however an underestimation as not all MSM with multiple partners are PrEP users About one third of mpox cases with a known HIV status reported not using PrEP at the time of mpox diagnosis. Moreover, people living with HIV are not included while HIV infection has been shown to be a risk factor for exposure to mpox. In Belgium, there are at least 19.000 people living with HIV in 2024. There are no official nor recent statistics on the number of sex workers in Belgium nor gender differentiation. The federal police estimated in 2015

that there are 26.000 sex workers. UTSOPI, the collective of sex workers in Belgium, uses an estimate of 25.000-30.000 (FPS Social Security Report).

Population immunity

Immunity against (severe) disease can be acquired through 1) previous infection (with assumed cross-protection for Clade Ib/sh2023 after infection with Clade IIb/sh2017) 2) recent mpox vaccination or 3) historical smallpox vaccination (people born before 1976 in Belgium).

Across 2022-2025, 921 **cases of mpox** have been reported in Belgium (of which 806 during the 2022 epidemic). In 2024-2025 there were 115 reported mpox cases. Of those, 14 (12.2%) had been previously vaccinated with two doses, and 4 with one-dose (3.4%). Two cases (1.7%) reported previous mpox.

A **seroprevalence of approximately 50%** (orthopoxvirus IgG) comprising natural and vaccine-induced immunity was identified among PrEP users at the Institute of Tropical Medicine after the 2022 mpox epidemic (4). However, it is unclear whether seroprevalence correlates with protection, whether these numbers still hold true today and to what extent these results are generalizable at the national level.

There is no exact information on vaccination coverage in the at-risk group. A 2024 internet survey among MSM (online recruitment to target sexually active population through MSM-targeted dating apps, social media and (inter)national HIV-LGBT organisations) identified that approximately **24% of Belgian respondents reported having been vaccinated** with two vaccine doses (1,5) However, it should be noted that due to convenience sampling, this percentage is likely to be biased and cannot be generalized to the entire Belgian MSM population.

Between January 2023 – September 2024, HIV reference centres reported the administration of 1831 Jynneos/Imvanex vaccine doses to the Federal Public Health Service. Of these, 551 were recorded as second doses, but information on number of doses was often missing. Some HIV reference centres such as Saint-Pierre and St Luc continue to vaccinate while others (Flemish region) have stopped. In addition, Santé Publique France has reported that at least 1,200 first doses and nearly 1,000 second doses of mpox vaccine were administered to Belgian residents in northern France (between Aug 22 2022 and May 15 2023).

The **basic reproduction number (R0)** of the **mpox Clade IIb/sh2017** 2022 epidemic across sexual networks was pooled and estimated at 2.44, with variability between EU countries (e.g. 2.32 in the UK and 2.82 in Germany) (6). Assuming Clade Ib/sh2023 has a comparable R0 as Clade IIb/sh2017 (within sex networks) of 2–3, this translates to a **herd immunity threshold of 50-67%** (HIT = 1 – 1/R0). However, estimation of the HIT assumes homogenous mixing in the at-risk population, which is not the case for transmission of sexually transmitted infections such as mpox, which is largely impacted by propagation through superspreaders with multiple high-risk contacts (7). In this context, natural/vaccine-induced immunity among people with multiple high-risk contacts is essential to prevent outbreaks.

Notably, in Belgium and the EU/EEA, low-level circulation of mpox Clade IIb/sh2017 cases among MSM has not resulted in a large outbreak since 2022 (8).

Risk of (inter)national dissemination
High

The previous Clade IIb/sh2017 outbreak in the EU clearly demonstrated the potential for international spread through sexual networks. A number of international events involving sexual networks of MSM functioned as superspreading events. Similarly, the current detection of autochthonous cases in multiple EU countries with a similar timing indicates that there is already undetected international spread. As such, the **risk of (inter)national dissemination is considered to be high but not expected to cause major outbreaks**.

An ECDC modelling study (pre-print) assessed the probability of an mpox Clade Ib/sh2023 outbreak in an MSM sexual network population of 10.000 in a metropolitan city. It modelled scenarios taking into account some population immunity (varying by

scenario), and varying transmissibility of Clade Ib/sh2023 (equal to or +15% higher than clade II) (9). The **simulations showed that the introduction of one undetected mpox case into a sexual network led to a high chance of a small outbreak** of >10 cases (probability 15-20%). However, one undetected introduction appeared **unlikely to lead to a large outbreak of >200 cases** (probability of 0.7-3.9%). In case of at least 10 undetected introductions and increased transmissibility of Clade Ib/sh2023 is the risk of a large outbreak (>200 cases) more than 50%. The simulations also showed that **targeting the top 15% most sexually active individuals**, even with a vaccination uptake increase of 5% (e.g. 1000 doses for 500 of 10.000 individuals) is critical to effectively limit outbreaks. A more detailed description of the results of the study are available in the Annex.

PREPAREDNESS & CONTROL MEASURES ALREADY IN PLACE

Preparedness

- **Contact tracing**

Mandatory notification and contact tracing for infection prevention and control is currently in place, with management guidelines described here. This led to the identification of 115 mpox cases in Belgium in 2024–2025.

- **Access to testing / diagnosis**

Since January 2025, testing and diagnosis capacity has been centralised within the National Reference Centre for mpox (link). PCR testing is available daily during the weekdays. There is a turnaround time (TAT) of approximately 7 days for clade subtyping (I, II, a, b), but can be performed the day after positive PCR result as necessary. The NRC for mpox performs genomic sequencing (TAT 7 days) on a subset of mpox samples upon request by the Health Authorities.
Information about procedures for sampling and transport for clinical laboratories is available on the webpage of the NRC (sampling procedures).
An update of the Royal Decree describing the mandate of National Reference Centres is in development in order to ensure a legal mandate and financing for upscaling and decentralisation of testing in case of an infectious disease epidemic that exceeds NRC laboratory capacity.

- **Vaccination**

Historical smallpox vaccination
Although there is limited evidence to assess vaccine effectiveness (VE) against clade I infection, the premise is that vaccinia vaccines offer **cross-protection** against diseases caused by other orthopoxviruses. The rise of mpox in African countries such as Nigeria coincided with the halt of routine smallpox vaccination in the 1980s (10). The earliest studies of first-generation smallpox VE against mpox infection during the 1980s identified VE estimates of **82-85%** (11–13). A more recent European study identified a slightly lower pooled first-generation smallpox **VE of 70%** (95% CI 23-89) during the 2022 Clade IIb/sh2017 epidemic.

Specific Mpox vaccination
Third generation mpox vaccines have demonstrated a **pre-exposure vaccine effectiveness** against mpox Clade IIb/sh2017 infection of 82% (95% CI 72-92) for two doses and 76% (95% CI 64-88) for one dose, based on studies performed in 2022-2023 (14). Of note is that one of the recent EU/EEA clade Ib/sh2023 cases was previously vaccinated, but reported only mild disease. **Post-exposure vaccination** can also be administered within four days after mpox exposure, however the VE is very low (20%, 95% CI -24–65) (14).

The latest mpox Vaccination Guidelines by the Superior Health Council (revised August 2022) are available here. Currently, there is no routine vaccination schedule in place to vaccinate at-risk groups.

- **Surveillance**

Mandatory notification data is sent to Sciensano for epidemiological surveillance and monthly reporting to ECDC. Case reporting through mandatory notifications collects

	information on vaccination status, clade, previous mpox infection, travel history, HIV status, symptoms, hospitalisation and death. In response to the 2024 Mpox Risk Assessment, wastewater surveillance was adapted to include mpox as a monitoring target, including clade subtyping. A retrospective analysis on wastewater samples for detection of mpox was performed in 2024 based on samples collected during the 2022 Clade IIb/sh2017 epidemic. Wastewater analyses detected mpox in Brussels during the peak of the outbreak (approx. 20 cases/week in Brussels). However, pathogen degradation over time leads to unmeasurable virus, which makes it difficult to assess at what threshold wastewater surveillance can detect mpox circulation in the population. - **Awareness** We consider awareness of the disease to be high among clinicians as mpox leads to a characteristic painful skin pox lesion. The 2022 Clade IIb/sh2017 epidemic led to widespread awareness of the disease in Belgium, with HIV Reference Laboratory associated clinics managing diagnosis, treatment and vaccination. Since then, mpox has remained as a mandatory notifiable disease and led to the detection of 59 cases in 2025, among which 5 mpox Clade Ib/sh2023 cases. Nevertheless some cases may go undetected as differential diagnosis with other infections such as herpes might be difficult.
Specific Control Measures *(surveillance, control, communication)*	In response to the ECDC threat assessment: - The National Reference Centre for mpox can perform genomic sequencing of the mpox Clade Ib/sh2023 case that occurred among a traveller returning from a non-endemic country and transmit the results to ECDC. - Testing of wastewater samples for mpox was initiated in the week of the 27th of October for the treatment plants in Antwerp, Brussels and Liège. - Communication to ID physicians is foreseen through the Flash Infectious Diseases of November

PUBLIC HEALTH IMPACT IN BELGIUM

Public Health Impact: *Low-medium*	Since the 2022 epidemic in Belgium, 115 mpox cases have been reported in 2024-2025 but not led to an outbreak. This could be explained by the combination of appropriate infection prevention and control measures limiting introduction into sexual networks and/or sufficient herd immunity that limits onwards transmission within at-risk populations. There are several uncertainties that will influence the public health impact - It is not yet known whether all the current autochthonous cases in the EU/EEA have a similar genotype, indicative of wider European transmission, or whether they represent different pockets of local transmission. Genomic sequencing and surveillance at the European and international level can help elucidate this question. - Transmissibility of Clade Ib/sh2023 compared to Clade IIb/sh2017 is currently unclear. - The degree of herd immunity among the at-risk population in Belgium and potential waning immunity. ITM is currently repeating a seroprevalence study among PrEP users.

RECOMMENDATIONS

Based off recent scientific evidence, the current EU/EEA and Belgian epidemiological situation, and taking into account current uncertainties, the following actions are proposed:

1. Maintain contact tracing to initiate infection prevention and control measures to prevent mpox introduction into or spread among sexual MSM networks. Sciensano is currently working on an advice for the Health Authorities, expected to be ready by the end of 2025.

2. Enhance surveillance to better understand the current epidemiological situation and extent of existing transmission of mpox among sexual MSM networks in Belgium.

- Improve data quality of **mandatory notifications**, in particular for information on immunity status (smallpox/mpox vaccination, previous mpox infection), type of exposure (sexual/household/healthcare contact, sexual behaviour) and travel history.
- **Perform genomic sequencing** of mpox cases with unclear origin (i.e. no epidemiological ties to an imported case from an endemic country, no identified source of infection). Sequence results shall be shared with ECDC or uploaded to international repositories to assess whether there are genomic-epidemiological links either between Belgian cases and 1) the EU/EEA cases (indicative of community transmission) or 2) (sporadically imported) international strains.
- **Wastewater surveillance** may temporarily complement the existing surveillance by identifying whether there is undiagnosed widespread circulation of mpox in the population, including clade differentiation Since the number of undetected cases influences the possible scale of an outbreak, such data can provide important epidemiological insights. Monitoring can be performed weekly across three metropolitan cities (Brussels, Liège, Antwerp) for the upcoming 4–8 weeks. An assessment will be performed after 4 weeks to assess whether relevant to continue thereafter.

3. Vaccination

- Request the **Belgian Superior Health Council** to review existing guidance on mpox vaccination in light of the current situation and newly available evidence;
- Clarify the available stocks of vaccines and ensure **sufficient stocks** are available to allow for unrestricted implementation of the (reviewed) vaccination recommendations;
- Improve **vaccination registration** in order to monitor how many vaccine doses people received (one-dose, two-dose, x-dose) and criteria for administration (preventive or post-exposure vaccination). Attention should be paid to ensuring confidentiality of information on sexual behaviour.

4. Communication

- Ensure harmonised communication across the regions and sectors.
- Clinicians and healthcare professionals (including clinical laboratories) should be made aware of the recent detection of locally acquired Clade Ib/sh2023 mpox cases across EU/EEA countries and informed of the necessity to notify Federated Health Authorities of suspected cases for contract tracing measures and send samples for laboratory testing to the National Reference Centre for mpox.
- Communication should be directed in particular at physicians working in **HIV-STI and PrEP clinics**.
- After healthcare professionals have been informed, community engagement and sensibilisation of **at-risk MSM groups** should be foreseen through HIV-STI prevention community based organisations.

ACTIONS

Sciensano

- Maintain wastewater surveillance for the following 4-8 weeks (or until clarity regarding spread of mpox Clade Ib/sh2023 in the EU);
- Further centralize epidemiological follow-up and reporting to international level.
- Communicate on the current epidemiological situation through the November newsflash of infectious diseases in order to improve awareness, detection and diagnosis for surveillance.

National Reference Centre for Mpox

- Maintain clade subtyping
- Perform genomic sequencing for mpox cases of unclear origin and upload sequences to international repository or share with ECDC (e.g. via GISAID) in order to assess whether the current circulation of genotypes is associated with onward transmission in EU/EEA or due to multiple importations from endemic countries.

FPS Public Health

- Ensure sufficient vaccine stocks at different levels and availability for vaccinators;
- Make official request to Superior Health Council to review vaccination guidelines;
- Update list of recognised clinical laboratories for mpox confirmation as it is no longer reimbursed by RIZIV-INAMI in 2025 (link).
- Send out communication to all HIV-STI and PrEP clinics.

Federated Health Authorities

- Maintain contact tracing capacities and transfer required information to Sciensano;
- Send out communication to general physicians;
- Notify Sciensano when an mpox case was transmitted through sexual networks without epidemiological ties to an endemic country (clade I or II);
- Ensure efficient individual registration of administered vaccinations (number of doses, indication for pre- or post-exposure vaccination) and assure data transmission to Sciensano;
- Distribute information to individuals at high risk through dedicated organisations for the prevention of STI and HIV and general communication.

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ANNEXES

Summary of main points of the pre-print article "Modelling the outbreak risk of monkeypox virus clade Ib among MSM in the EU/EEA and the impact of targeted vaccination"
Available from: http://medrxiv.org/lookup/doi/10.1101/2025.07.04.25330877

Risk of a small or large outbreak

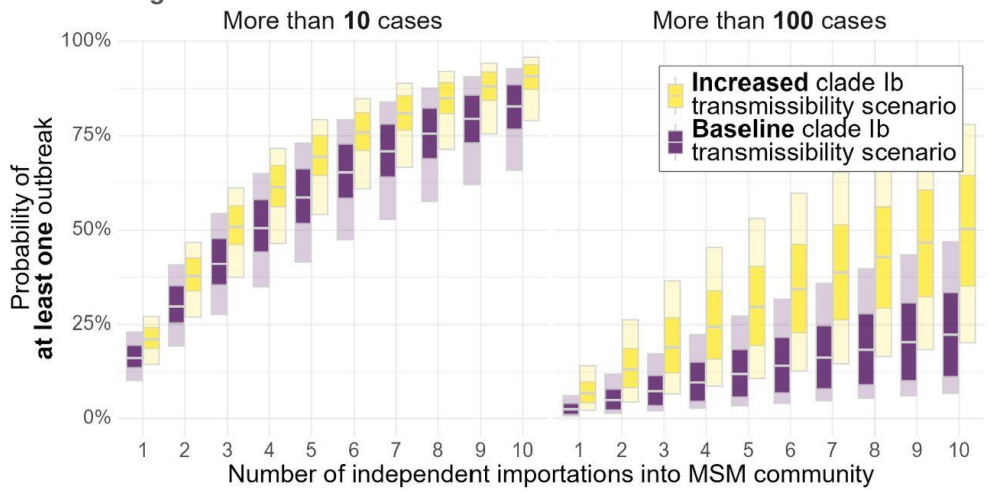
The simulations indicated that one singular undetected importation into a sexual MSM network is likely to lead to small outbreaks (>10-20 cases: probability 15.0 – 20.3%), but not to large outbreaks (>200 cases: 0.7 – 3.9%). In the increased transmissibility scenario, the probability of large outbreaks is higher, with less of an impact on the probability of smaller outbreaks.

Table 1. Probability of different outbreak sizes depending on clade Ib transmissibility scenarios

Outbreak size (cumulative incidence threshold)	Outbreak probability (baseline transmissibility scenario)	Outbreak probability (increased transmissibility scenario)
More than 10 detected cases	15.0% [9.6-21.7%]	20.3% [13.7-25.6%]
More than 20 detected cases	10.4% [5.6-14.2%]	15.4% [9.6-19.3%]
More than 50 detected cases	5.2% [2.4-8.5%]	9.7% [5.1-15.4%]
More than 100 detected cases	2.5% [0.7-6.1%]	6.7% [2.2-14.0%]
More than 200 detected cases	0.7% [0.0-3.5%]	3.9% [0.6-12.2%]
More than 500 detected cases	0.0% [0.0-0.0%]	0.1% [0.0-1.0%]

The probability of small or large outbreaks increases with additional undetected importations of mpox clade Ib into a sexual MSM network (Figure 1). Each additional undetected importation increases the risk of small or large outbreaks, with the scenario of increased clade Ib transmissibility having the most impact on the probability of a large outbreak (cfr plot 2).

Figure 1. Probability of subsequent undetected mpox clade Ib importation into sexual MSM network leading to small or large outbreaks



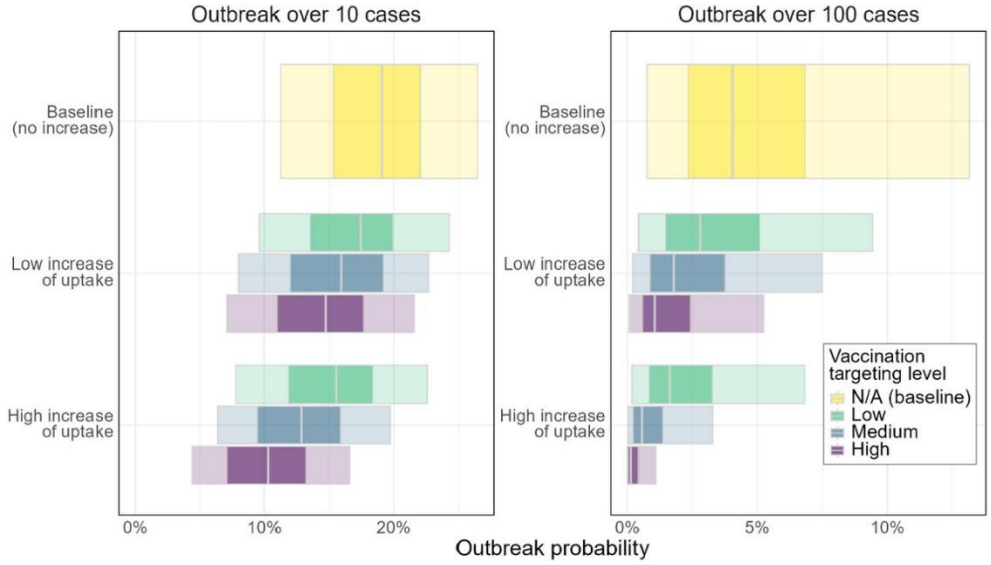
Impact of targeted vaccination

The impact of targeted vaccination on small (>10 cases) and large outbreaks (>100 cases) was analysed with different scenarios: an increased vaccination uptake of 2,5% (low) and 5% (high) among different target groups of sexually active people: top 15% (high), 25% (medium) and 50% (low).

The baseline probability of is 19.1% for small and 4.0% for large outbreaks. In both scenarios of low (+2.5%) or high vaccine uptake (+5%), targeting the top 15% most sexually active individuals is critical to effectively limit outbreaks (cfr. purple box plots) compared to a broader non-targeted vaccine uptake among 50% of

the at-risk population (green box plot). The impact of increasing vaccination uptake of 5% appears to be more effective in limiting small and large outbreaks, while increasing uptake by 2.5% has less of an impact on the probability of smaller outbreaks.

Figure 2. Probability of small or large outbreaks from a singular imported case, depending on vaccination uptake among different targeted sexually active groups



Dark and light bars indicate the 50% and 95% confidence intervals. Note the different x-axes between the two plots.

An increase in vaccination uptake among the top most sexually active individuals will be most effective in limiting outbreaks. In these scenario, an increase in vaccination requires approximately 500 doses (+2.5% uptake) or 1000 doses (+5% uptake, 2 doses for 500 of 10.000 individuals).

DESCRIPTION METHODOLOGY	
EVIDENCE	
AVAILABILITY OF EVIDENCE	The sources used for this risk assessment have been duly referenced. As indicated in the text on 'public health impact' several currently unknown factors could influence the potential public health impact.
EXPERTS	
SELECTION PROCESS	Experts that have been involved in previous risk assessments on the same topic were invited to contribute to this RA. They were selected based on relevant expertise, motivation, geographical and language representativeness. Additionally, permanent RAG members (as defined by the protocol agreement) were involved.
EXPERT LIST	Leila Belkhir (St Luc), Valentin Blaison (ExAequo), Koen Blot (Sciensano), Steven Callens (UZ Gent/NITAG), Laura Cornelissen (Sciensano), Steven De Keukeleire (RZ Tienen), Marie-Angélique De Scheerder (UZ Gent), Pierre-Louis Deudon (FAMGB/CMG), Wouter Dhaeze (DZ), Achille Djena (AVIQ), Naima Hammami (DZ), Niel Hens (U Hasselt/U Antwerp), Bart Hoorelbeke (FOD), Hilde Janssens (UZ Antwerp), Amaryl Lecompte (Sciensano), Laurens Liesenborghs (ITM), Agnes Libois (CHU St Pierre), Charlotte Martin (CHU St Pierre), Christelle Meuris (CHU Liège), Geert Molenberghs (U Hasselt/KU Leuven), Annick Paeps (DZ), Sophie Quoilin (CHU St Pierre), Florence Rolin (Vivalis), Anna Schmelz (GSC), Anne Simon (SHC), Patrick Soentjens (ITM), Stefan Teughels (Domus Medica), Marjan Van Esbroeck (ITM), Marc Van Ranst (UZ Leuven), Koen Vercauteren (ITM)
DECLARATION CONFLICT OF INTEREST	All experts that have submitted a DOI have been assessed by the RAG coordination team. No relevant conflicts were disclosed. An ad-hoc DOI will be requested from those experts who did not yet submit a DOI.
CONSULTATION PROCESS	
MEETING	Draft Risk Assessment sent to RAG experts on 31/10/2025 Online expert meeting on 04/11/2025 Final draft approved via mail on 5/11/2025 Final RA published on 5/11/2025 Final RA sent to RMG on 5/11/2025
DECISION PROCESS	
CONSENSUS	Consensus was reached among the experts about the Risk Assessment and its recommendations. No major objections were raised.
OBJECTIONS	None