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SARS-COV-2 VARIANT EVOLUTION: GLOBAL PATTERNS, NEW SUBVARIANTS, AND REGIONAL CONTEXT (UKRAINE & HIV)

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Since late 2019, SARS-CoV-2 has diversified into numerous lineages, driving recurrent global waves of COVID-19. This narrative review synthesizes evidence on the evolutionary dynamics of SARS-CoV-2 with emphasis on Omicron subvariants, including JN.1 and its descendants, and emerging 2025 lineages (Nimbus and Stratus).

We summarize major mechanisms shaping viral diversification – mutation/antigenic drift, recombination, and prolonged infection in immunocompromised hosts (including people living with HIV) – that can promote stepwise accumulation of immune-escape mutations.

The review covers literature and genomic surveillance reports from 2019–2025 (WHO resources, GISAID, outbreak.info, PubMed/Scopus) and focuses on mutation profiles of key variants, global prevalence trends, and Ukraine-specific context.

A dedicated section addresses why Ukraine – despite a relatively high HIV burden in Eastern Europe – has not been recognized as a major source of globally dominant variants of concern. Contributing factors discussed include limited sequencing coverage, reduced travel/export potential, expansion of ART, and stochastic and structural determinants required for widespread dissemination of newly arising lineages.We conclude that ongoing immune escape remains likely, underscoring the need for robust genomic surveillance, timely vaccine/therapeutic updates, and integration of COVID-19 monitoring with HIV services.

Keywords: *SARS-CoV-2; variants of concern; Omicron; JN.1; BA.2.86; recombination; immune escape; genomic surveillance; Ukraine; HIV; immunocompromised hosts; antiretroviral therapy.*

The COVID-19 pandemic has been characterized by waves of infection driven by successive SARS-CoV-2 variants of concern (VOCs). Since the ancestral Wuhan-Hu-1 strain was first described in December 2019, the virus has diversified into thousands of lineages [1, 2]. Among them, Alpha (B.1.1.7), Delta (B.1.617.2), and Omicron (B.1.1.529 and its sublineages) have produced the largest global surges, with Omicron establishing prolonged dominance since late 2021 [2–5]. By 2023, subvariants such as XBB.1.5 and JN.1 achieved global dominance[5, 6] displaying enhanced transmissibility and immune escape [7–10]. In 2025, descendants of JN.1 continued to diversify, raising concerns about reinfection and vaccine breakthroughs.The global dominance of Omicron JN.1 by late 2023, followed by the emergence of Nimbus and Stratus in 2025, underscores that SARS-CoV-2 remains on a trajectory of ongoing immune escape and adaptation. These lineages are currently under active surveillance by the World Health Organization (WHO) and genomic consortia such as GISAID [1, 11, 12]. There is substantial evidence suggesting a connection between the emergent variant of Omicron and immunocompromised status due to cancer or HIV [13]. The high prevalence of HIV infection and AIDS in South Africa may have contributed to the emergence of the Omicron variant. This situation is markedly different from that in other countries [13–15]. The emergence of new SARS-CoV-2 variants is a global phenomenon driven mainly by the natural processes of viral mutation and natural selection, especially in regions with high infection rates and varying levels of population immunity.

Interestingly, countries in Eastern Europe, despite having high rates of immunocompromising conditions like HIV, have not consistently produced new Variants of Concern (VOCs) [13, 16]. While these nations have faced high COVID-19 cases and mortality—often due to low vaccination rates and weaker health systems—there is no evidence of them generating major VOCs that achieved global dominance [15, 16].

Key VOCs detected:

– Alpha (B.1.1.7) – UK
– Beta (B.1.351) – South Africa
– Gamma (P.1) – Brazil
– Delta (B.1.617.2) – India
– Omicron (B.1.1.529) – Botswana and South Africa

Ukraine serves as a notable example [16, 17].

This review aims to summarize the mechanisms shaping SARS-CoV-2 evolution, provide updated data on the prevalence of major variants, including Nimbus and

Stratus, and analyze why Ukraine's immunological vulnerability does not lead to variant emergence.

Methods

We conducted a narrative review of peer-reviewed literature, preprints, and genomic surveillance reports (2019–2025), using databases such as WHO COVID-19 Dashboard, outbreak.info PubMed-indexed studies (2020–2025), Scopus, and GISAID [1, 17–21]. Inclusion criteria focused on empirical studies of SARS-CoV-2 evolution, immune evasion, and HIV prevalence in Eastern Europe. Data extraction centered on mutation profiles, variant prevalence, and Ukraine-specific dynamics.

Inclusion criteria were:

1. Peer-reviewed original research or preprints describing SARS-CoV-2 evolution, immunological escape, or variant epidemiology.

2. WHO, UNAIDS, or national reports on HIV prevalence and antiretroviral therapy (ART) coverage in Eastern Europe and Central Asia.

3. Genomic surveillance reports relevant to Ukraine and neighboring countries.

We excluded purely modeling studies without empirical data, duplicate datasets, and non-English articles unless translations were available. References were managed using Mendeley.

Data extraction focused on:

- Mutation profiles of major VOCs.
- Documented mechanisms of immune evasion.
- Prevalence trends by region (2019–2025).

The descriptive analyses and visualizations were created to summarize trends and mechanisms reported by the WHO, european centre for disease prevention and control (ECDC), centers for disease control and prevention (CDC), global initiative on sharing all influenza data (GISAID), and UNAIDS. Figures 1–4 were created using computer-based data processing and standard plotting tools, resulting in comparative bar and line charts, as well as schematic diagrams that illustrate the key concepts of viral evolution and variant emergence.

Mechanisms of Evolution

Mutation and Immune Selection

SARS-CoV-2 accumulates mutations at ~1×10^{-3} substitutions/site/year, shaped by replication errors and host immunity [4]. Key mutations in the spike protein (N501Y, L452R, F486P) alter ACE2 affinity or antibody binding [6, 7]. Convergent evolution has produced recurring substitutions across lineages, reflecting strong immune selection.

Antigenic drift

Spike receptor-binding domain (RBD) substitutions such as N501Y, L452R, and F486P/L repeatedly arose across lineages under antibody pressure [3, 5–7].

Recombination

Lineages like XBB emerged from BA.2 recombinants, combining escape features [9,12]. Other factors [4, 17, 18], such as prolonged infection and immunocompromised patients, including those with advanced HIV, can harbor the virus for months with stepwise spike mutations converging with VOCs (Fig. 1).

Prolonged Infection in Immunocompromised Hosts

Notably, case reports from South Africa and the U.S. have documented prolonged SARS-CoV-2 infection in immunocompromised HIV-positive individuals, leading to high intra-host mutation rates [22–24].

Immune Pressure and Vaccine Escape

Neutralizing antibodies, whether elicited by infection or vaccination, exert strong selective pressure [7, 8]. The appearance of convergent RBD substitutions (e.g., E484K, K417N, N501Y) across unrelated lineages illustrates immune-driven adaptation.

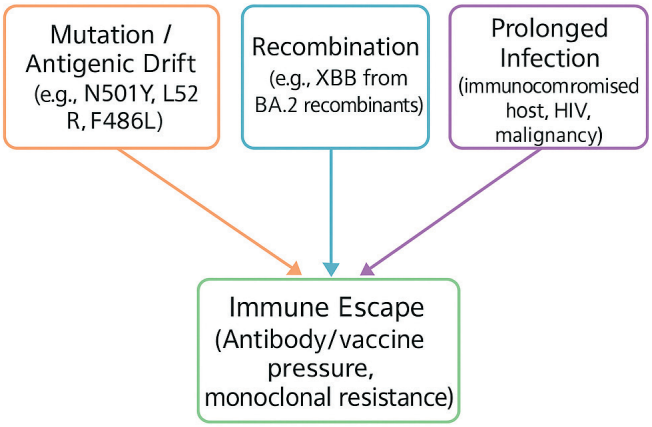

Fig. 1. Mechanisms of SARS-CoV-2 evolution. Adapted from Harvey et al. [3], Choi et al. [22], Clark et al. [23], Kovalenko, V. et al. [24].

This schematic diagram illustrates three major processes driving SARS-CoV-2 evolution: mutation/antigenic drift, recombination, and prolonged infection in immunocompromised hosts. Each mechanism contributes to the accumulation of genetic changes that facilitate immune escape under selection pressures such as vaccination, prior immunity, and monoclonal antibody use.

Global Variant Landscape (2020–2025)

Alpha (UK, 2020) carried N501Y, increasing transmissibility [2, 3]. Delta (India, 2020) carried L452R, P681R, outcompeted Alpha globally [3]. Omicron BA.1 (South Africa, 2021) had >30 spike substitutions [4–6] and high immune escape (Table 1). BA.5 added L452R, F486V [7, 8]. XBB lineages emerged in 2022 from BA.2 recombination with enhanced immune escape [9, 10].

BA.2.86 (Pirola) in 2023 carried >30 new spike substitutions [10–12]. JN.1 (late 2023) became dominant globally [1, 11, 16, 19, 24].

Figure 2 illustrates the global prevalence trends of SARS-CoV-2 variants from Alpha to JN.1, providing a stylized representation of their relative prevalence from 2020 to early 2025.

This figure presents the temporal dynamics and relative global prevalence of major SARS-CoV-2 variants based on patterns reported by WHO, GISAID, and global genomic surveillance networks. The trajectories are schematic and intended to illustrate the sequential emergence, dominance, and replacement of variants over time, rather than display exact quantitative prevalence values.

Table 1

Comparative Features of Major SARS-CoV-2 Variants

Variant	First Detection	Key Spike Mutations	Immune Escape	Transmissibility	Clinical Impact
Alpha (B.1.1.7)	UK, 2020	N501Y	Moderate	↑	Hospitalization ↑
Delta (B.1.617.2)	India, 2020	L452R, P681R	Moderate–High	↑↑	Severe
Omicron BA.1	South Africa, 2021	>30 spike	High	↑↑↑	Immune escape
BA.5	South Africa, 2022	L452R, F486V	High	↑↑↑	Immune escape
XBB.1.5	Global, 2022	F486P, R346T	High	↑↑↑	Immune escape
BA.2.86	Global, 2023	>30 new spike	High	↑↑	Potential escape
JN.1	Global, 2023	F456L	High	↑↑↑	Dominant

Sources: WHO COVID-19 Dashboard [1], GISAID [11], Viana et al. (2022) [4], Cao et al. (2022) [7], Tamura et al. (2023) [9].

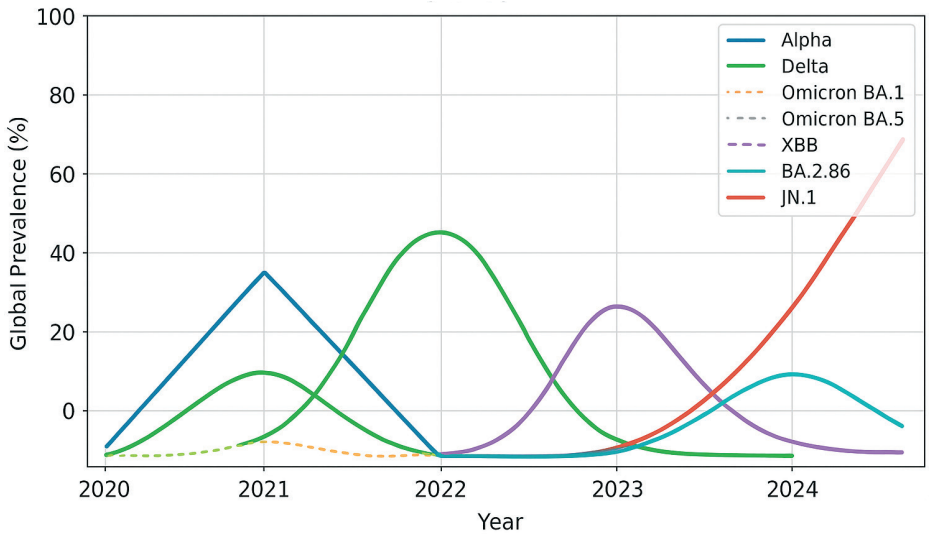

Fig. 2. Schematic representation of global SARS-CoV-2 variant prevalence, 2020–2025. Based on WHO [1], ECDC [12, 16], CDC [19], and GISAID [11].

Regional Context: Ukraine & HIV

Ukraine has one of the highest HIV prevalence rates in Eastern Europe [24–26]. Despite this, Ukraine has not been identified as a source of globally significant variants .

Possible contributing factors include: limited sequencing coverage [11, 12, 16, 24], reduced travel/export potential after 2021 [16], expansion of ART [13–17], and stochastic effects: emergence of globally dominant lineages requires both virological and epidemiological conditions [2, 3, 9].

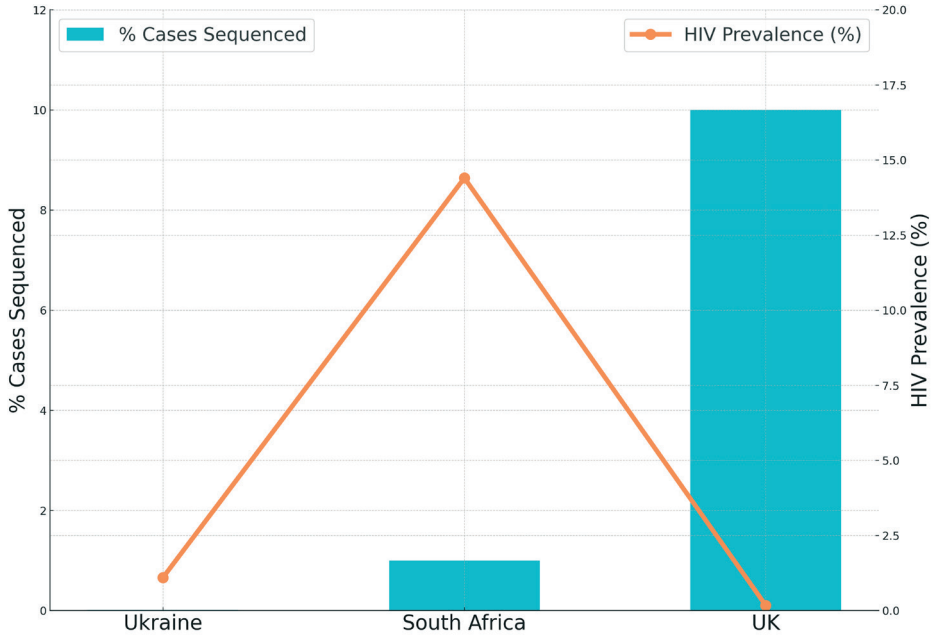

Fig. 3. Regional comparison of sequencing coverage vs HIV prevalence (schematic). Based on WHO [1], UNAIDS [21], and ECDC [16].

This schematic figure uses real-world estimates (2020–2021) to illustrate the relationship between national SARS-CoV-2 genomic sequencing coverage and HIV prevalence. HIV prevalence among adults aged 15–49 years was sourced from UNAIDS/WHO country-level reports, while sequencing coverage reflects published analyses of SARS-CoV-2 genome submissions relative to reported COVID-19 cases during the same period. Countries shown include Ukraine (1.10% HIV prevalence; 0.012% of cases sequenced), South Africa (14.4%; ~1%), and the United Kingdom (0.17%; ≥10%). These data highlight striking global inequalities in genomic surveillance capacity, with countries experiencing a high burden of HIV often reporting substantially lower sequencing coverage.

Discussion

Omicron and its descendants illustrate how SARS-CoV-2 continues to adapt through convergent spike changes [3, 5–7]. XBB recombinants and BA.2.86 show that large antigenic shifts remain possible [9, 10]. By 2024–2025, JN.1 and its descendants dominated global circulation [1, 16, 19]. The Ukrainian paradox – a high HIV prevalence setting that did not generate major global VOCs – illustrates the complexity of variant emergence. While immunocompromised hosts are necessary for long-term intra-host evolution [22, 23, 27, 28], successful global spread depends equally on sequencing capacity, transmission intensity, and travel connectivity [29]. South Africa's role in the emergence of Beta and Omicron underscores the importance of high background transmission and strong genomic surveillance systems that can detect and amplify new lineages [5, 39]. Ukraine's limited sequencing capacity (<0.2% of cases sequenced by 2023) and reduced international travel after 2022 [24, 26, 28] likely restricted the probability that locally arising lineages would seed globally dominant variants (Fig. 4).

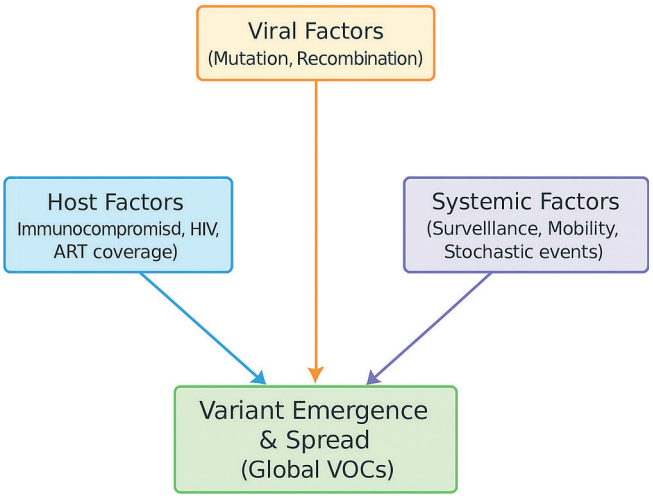

Fig. 4. Conceptual model of drivers of SARS-CoV-2 variant emergence. Adapted from WHO [1], Rambaut et al. [2], UNAIDS [21], Kovalenko, V. et al. [24].

This Conceptual model reflects an interplay of viral adaptation, host immunity, and systemic factors. Future waves driven by immune escape are likely. Monitoring systems require robust genomic surveillance, vaccine updates, and integration with HIV services [1, 3, 6, 7, 10, 11, 13, 16, 19].

Conclusion

The evolution of SARS-CoV-2 since 2019 highlights a complex interplay between viral biology, host immunity, and societal factors. Variants such as Alpha, Delta, and Omicron have demonstrated the virus's ability to mutate and evade the immune response. By late 2023, the Omicron JN.1 variant had become dominant, followed by the emergence of the Nimbus and Stratus variants in 2025. From a global health perspective, three key lessons can be drawn:

1. Robust genomic surveillance is essential for early detection; however, coverage can be uneven across different regions.

2. Vaccine adaptation and therapeutic innovation are vital for maintaining protection against severe disease, as the effectiveness of vaccines against symptomatic infection has decreased for newer variants.

3. The situation in Ukraine, characterized by a high prevalence of HIV but low variant emergence, illustrates that viral evolution is not solely influenced by host factors; structural issues also play a significant role.

Looking ahead, SARS-CoV-2 is likely to persist as an endemic pathogen, with the potential for future disruptions due to immune escape. Preparedness should involve multi-layered surveillance, the development of broad immunological tools, and strategies that address multiple diseases.

Ultimately, a globally coordinated yet regionally adaptable response is necessary. It is crucial to learn from both high-surveillance and under-resourced areas. Vigilance, adaptability, and equity will be key in addressing future viral evolution.

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ЕВОЛЮЦІЯ ВАРІАНТІВ SARS-COV-2: ГЛОБАЛЬНІ ЗАКОНОМІРНОСТІ, НОВІ СУБВАРІАНТИ ТА РЕГІОНАЛЬНИЙ КОНТЕКСТ (УКРАЇНА ТА ВІЛ)

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РЕЗЮМЕ. З кінця 2019 р. SARS-CoV-2 еволюціонував у велику кількість ліній, що зумовило повторювані хвилі COVID-19 у світі. У цьому огляді узагальнені сучасні відомості про еволюційну динаміку SARS-CoV-2 з особливим акцентом на субваріантах Omicron, зокрема JN.1 та його похідні, а також на нових лініях, що з'являються у 2025 р. (Nimbus і Stratus).

Окреслено ключові механізми, які зумовлюють різноманіття вірусу, – мутації та антигенний дрейф, рекомбінацію, а також тривалу персистенцію збудника в імунокомпрометованих осіб (у тому числі людей, які живуть з ВІЛ). Саме ці процеси можуть сприяти поетапному накопиченню мутацій, що забезпечують вислизання від імунної відповіді.

Огляд охоплює наукові публікації та звіти з геномного нагляду за 2019–2025 рр. (ресурси ВООЗ, GISAID, outbreak.info, PubMed/Scopus) і зосереджується на мутаційних профілях ключових варіантів, глобальних тенденціях їх поширення і специфічному для України контексті.

Окремий розділ присвячено аналізу причин, чому Україна, попри відносно значний тягар ВІЛ у Східній Європі, не розглядається як значуще джерело глобально домінантних варіантів, що викликають занепокоєння. Серед можливих пояснень обговорюються обмежене секвенування, нижчий потенціал міжнародного поширення, розширення доступу до антиретровірусної терапії, а також випадкові й структурні чинники, необхідні для масового розповсюдження нових вірусних ліній.

У підсумку приходимо до висновку, що подальше уникнення імунної відповіді залишається ймовірним, що підкреслює потребу в ефективному геномному нагляді, своєчасному оновленні вакцин і терапевтичних підходів, а також в інтеграції моніторингу COVID-19 із програмами допомоги людям, які живуть з ВІЛ.

Ключові слова: *SARS-CoV-2, варіанти, що викликають занепокоєння, Omicron, JN.1, BA.2.86, рекомбінація, уникнення імунної відповіді, геномний нагляд, Україна, ВІЛ, імунокомпрометовані пацієнти, антиретровірусна терапія.*

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У ВИДАВНИЦТВІ «УКРМЕДКНИГА» ВИЙШЛА НОВА КНИГА!

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У навчальному посібнику висвітлено сучасні уявлення про причини активізації кліщових інфекцій та появу нових нозологічних форм. Ґрунтовно описано дев'ять найбільш розповсюджених хвороб людини із наведенням найновіших наукових даних (Лайм-бореліоз, гранулоцитарний анаплазмоз людини, бабезіоз та інші). Відомості про кожну інфекцію містять основні дані щодо історії її відкриття, актуальності, етіології, епідеміології, патогенезу, клінічних проявів, діагностики, лікування і профілактики, а також тестові питання для самоконтролю отриманих знань.

Для студентів медичних університетів, інтернів, епідеміологів, інфекціоністів і сімейних лікарів.

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