Review

Schmallenberg virus at 15: Lessons Learned and the Unanswered Questions in a Changing Climate

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Schmallenberg virus at 15: Lessons Learned and the Unanswered Questions in a Changing Climate

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Abstract

Schmallenberg virus (SBV) has evolved from an emergent *Orthobunyavirus* identified in Europe in 2011 into an endemic pathogen with complex epidemiological dynamics. This review synthesizes advances in SBV research over the past 15 years, focusing on molecular pathogenesis, transmission ecology, and control strategies. We highlight the NSs protein as a key interferon antagonist, the mechanisms underlying fetal neurotropism, and the influence of climate change on *Culicoides* vector biology. Recent evidence of winter vector activity challenges traditional assumptions of transmission seasonality, with implications for disease management and trade regulations. Advances in diagnostics and vaccine development—including DIVA-compatible and mRNA platforms—are critically evaluated, highlighting progress and persistent implementation gaps. Finally, we propose SBV as a model system for understanding arbovirus persistence and emergence in temperate regions within a One Health framework.

Keywords: *Schmallenberg virus*; *Orthobunyavirus*; *Culicoides*; arbovirus; climate change; congenital malformations; vaccine; epidemiology

1. Introduction: The Schmallenberg Decade and Beyond

1.1. Historical Emergence and Initial Spread

Since its identification in 2011, *Schmallenberg virus* (SBV) has provided a unique opportunity to study the emergence, spread, and establishment of a novel arbovirus in a temperate ecosystem. Unlike many arboviruses historically restricted to tropical regions, SBV demonstrated that climatic and ecological conditions in Europe are sufficient to sustain rapid viral expansion and long-term persistence [1,2]. The virus was first detected in blood samples from dairy cows in the Schmallenberg region of Germany during an investigation into fever, decreased milk production, and diarrhea in adult cattle. Metagenomic analysis identified a novel *Orthobunyavirus* of the *Simbu* serogroup (family *Peribunyaviridae*, order *Bunyavirales*). Within months, SBV spread explosively across Europe, becoming one of the most significant emerging livestock pathogens of the twenty-first century [3].

1.2. The Clinical Dichotomy

SBV infection presents a striking clinical dichotomy. In post-natal animals, infection is typically mild or subclinical, characterized by transient fever, decreased milk production, diarrhea, and reduced appetite—signs that are economically important but self-limiting [4]. The true pathogenic significance lies in its teratogenic potential. When naive pregnant ruminants are infected during a critical gestational window (approximately 28–56 days in small ruminants and 80–150 days in cattle), vertical transmission leads to severe fetal malformations, collectively termed arthrogryposis-hydranencephaly syndrome. These include muscular hypoplasia, fixed limb contractures

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(arthrogryposis), torticollis, and cavitating brain lesions such as porencephaly or hydranencephaly, often resulting in abortion, stillbirth, or the birth of non-viable offspring [5].

1.3. SBV as a Model Pathogen

Intensive research following the emergence of SBV has established it as an important model for studying orthobunyaviruses [3]. The development of reverse genetics systems and experimental models has provided a framework for responding to future arbovirus threats [6]. In this review, we argue that SBV now serves as a sentinel pathogen, reflecting the interplay between viral evolution, climate-driven vector expansion, international livestock trade, and the application of modern biotechnology to infectious disease control. Recent evidence of year-round *Culicoides* activity [7] further underscores its relevance as a model for climate-sensitive arboviruses.

2. Virology and Pathogenesis: New Insights into Old Questions

2.1. Genomic Organization and Molecular Virology

SBV possesses a tripartite negative-sense single-stranded RNA genome typical of *Orthobunyavirus* [8]. The large (L) segment encodes the RNA-dependent RNA polymerase (L protein), essential for viral transcription and replication. The medium (M) segment encodes a polyprotein precursor that is post-translationally cleaved into the surface glycoproteins Gn and Gc and the non-structural protein NSm. The small (S) segment employs an overlapping reading frame to encode both the nucleocapsid protein (N) and the non-structural protein NSs [9]. Gn and Gc mediate viral attachment and pH-dependent membrane fusion and represent the primary targets of the neutralizing antibody response.

2.2. The NSs Protein: A Master of Immune Evasion

Reverse genetics systems developed shortly after the emergence of SBV enabled dissection of virulence determinants. Varela et al. [10] demonstrated that the NSs protein functions as a major virulence factor by antagonizing the host type I interferon (IFN) response. A deletion mutant lacking NSs (SBVΔNSs) was markedly attenuated, confirming the essential role of NSs in immune evasion. The mechanism involves interference with cellular transcription machinery, blocking expression of IFN and interferon-stimulated genes. This strategy is conserved among many orthobunyaviruses and explains how SBV establishes systemic infection despite host antiviral defenses [8].

2.3. Neurotropism and the Pathogenesis of Congenital Malformations

The teratogenic effects of SBV result from its tropism for neuronal tissues in the developing fetus. In experimental models and naturally infected fetuses, SBV antigen is detected predominantly in neurons of the grey matter in the brain and spinal cord [10]. Neuronal infection leads to cerebral malacia and vacuolation of the cerebral cortex. Importantly, muscular hypoplasia characteristic of SBV-affected newborns is considered secondary to central nervous system damage rather than direct viral infection of muscle tissue. Viral destruction of spinal cord motor neurons disrupts neural input, causing neurogenic atrophy and arthrogryposis, a pathogenesis similar to that described for *Akabane virus* [5,11] (Figure 1).

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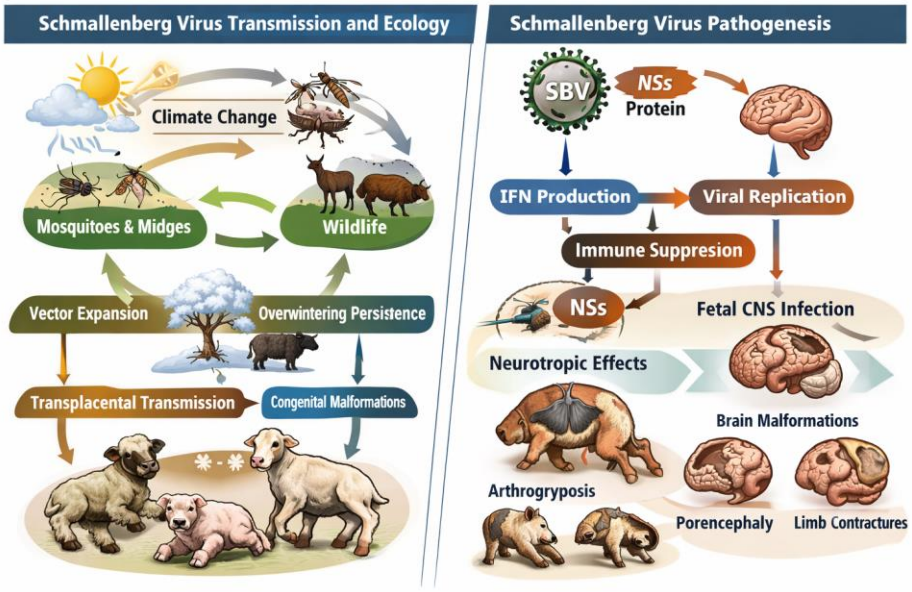

Figure 1. SBV transmission and pathogenesis. Schematic of SBV transmission (*Culicoides*–host–environment) and pathogenesis including NSs-mediated interferon suppression and fetal CNS damage.

2.4. Gestational Timing and Lesion Distribution

The nature and severity of SBV-induced lesions depend critically on the timing of fetal infection. Early infections cause severe brain cavitation, whereas later infections predominantly result in arthrogryposis [5,12]. For SBV and related *Simbu* serogroup viruses, infections in cattle between approximately 80–120 days of gestation typically produce porencephaly or hydranencephaly; infections between 120–180 days result in arthrogryposis; later infections may cause encephalomyelitis with calves born alive but showing flaccid paralysis or incoordination. A useful differential diagnostic feature is the virtual absence of cerebellar lesions in *Simbu* serogroup infections, distinguishing them from *Bovine Viral Diarrhea Virus* infection [5].

3. Epidemiology and Transmission: The Vector-Host-Climate Triad

3.1. The Culicoides Vector

SBV is transmitted almost exclusively by biting midges of the genus *Culicoides* (Diptera: *Ceratopogonidae*), making it a true arbovirus [6]. After an infected midge takes a blood meal from a susceptible ruminant, the virus replicates within the insect, undergoes an extrinsic incubation period of approximately 8–10 days, and is excreted in saliva during subsequent feeding. In Europe, multiple *Culicoides* species have been implicated, including members of the *Culicoides obsoletus* and *Culicoides pulicaris* complexes [13]. Notably, European vector species show greater tolerance to cooler temperatures than tropical counterparts, enabling SBV transmission at higher latitudes and altitudes.

3.2. Climate Change as a Driver of Transmission Dynamics

Climate change alters transmission dynamics by extending vector activity and enabling overwintering. Warmer temperatures accelerate viral replication within the vector, shorten the extrinsic incubation period, and increase the proportion of infectious midges [14]. Extended summers and milder autumns prolong vector activity, while reduced winter mortality allows overwintering of infected midges [6,15].

Recent empirical evidence from Germany challenges the concept of a "vector-free period" during Central European winters. Groschupp et al. [7] collected over 32,000 *Culicoides* midges during winter months (October to April), with more than 60% captured inside livestock buildings.

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Approximately 2,000 of these midges had recently taken a blood meal, nearly 95% of them inside stables. Midge activity was recorded at mean temperatures of 7.4 °C and a minimum of 0.3 °C. These findings suggest that indoor stable environments provide refugia that enable winter feeding and potentially continuous virus transmission, warranting reconsideration of trade regulations based on a vector-free period.

3.3. Globalization and Trade

International livestock trade represents a major driver of SBV dissemination. The initial European epidemic demonstrated how rapidly a novel arbovirus can spread through naive ruminant populations in regions with competent vectors. Seropositivity to SBV has been reported outside Europe, including Ethiopia and China, although viral presence has not been confirmed in all cases [6]. Enhanced border biosecurity, monitoring of live animal and germplasm trade, and early-warning systems in disease-free areas remain essential.

3.4. Endemic Stability and Wave-like Re-Emergence

Following the initial pandemic wave (2011–2013), SBV established an enzootic status in Central Europe characterized by periodic wave-like re-emergence [3,6]. This pattern reflects herd immunity dynamics: as the proportion of immune animals declines due to the birth of susceptible offspring and waning antibody titers, conditions favor renewed transmission when vector activity resumes. In endemic areas, most ruminants are infected at an early age and develop long-lasting immunity, making congenital abnormalities rare. However, extended warm summers can facilitate spread beyond usual ranges, and outbreaks of congenital infection can occur at the northern or southern limits of vector distribution [6].

4. Diagnosis and Control: From Reaction to Precision

The response to SBV over the past 15 years reflects a broader transition in veterinary medicine: from reactive outbreak management toward precision tools for surveillance, diagnosis, and targeted control. This section synthesizes current capabilities and persistent gaps.

4.1. The Diagnostic Toolbox

Accurate and timely diagnosis is essential for clinical management, surveillance, trade certification, and outbreak investigation. Diagnostic approaches have evolved to address the distinct phases of SBV infection—acute postnatal infection and congenital malformations—as well as the need for serological surveillance.

4.1.1. Molecular Detection

Reverse transcription quantitative PCR (RT-qPCR) remains the gold standard for detecting SBV RNA during the acute phase of infection. Viraemia in adult ruminants is typically short-lived (2–5 days post-infection), making timing of sample collection critical [16]. Whole blood (EDTA) is the preferred sample for acute cases; however, in cases of congenital infection, viral RNA can be detected in fetal tissues—particularly brain, spinal cord, and meconium—even when the dam is no longer viremic [12,17].

Multiplex and real-time RT-PCR assays have been developed to simultaneously detect and differentiate SBV from other teratogenic *Simbu* serogroup viruses (*Akabane*, *Aino*, *Shamonda*) and clinically similar pathogens (e.g., *Bovine viral diarrhea virus*, *Border disease virus*). Lee et al. [18] described a one-step multiplex RT-qPCR with detection limits of 2.4 copies for SBV, 96.2 copies for *Akabane*, and 52.3 copies for *Aino*, enabling rapid differential diagnosis in regions where multiple arboviruses co-circulate.

Next-generation sequencing (NGS) has emerged as a powerful tool for outbreak investigation and genomic surveillance. Metagenomic approaches can detect SBV without prior knowledge of the

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pathogen, as demonstrated during the initial discovery of the virus [1]. NGS also enables monitoring of viral evolution, identification of reassortment events, and tracking of introduction routes, contributing to early warning systems [6,19].

Challenges: The short viremic window limits the utility of molecular tests for retrospective diagnosis of congenital cases. Furthermore, the availability of RT-qPCR capacity varies across regions, and standardized protocols for sample handling and interpretation remain a priority for international harmonization.

4.1.2. Serological Assays

Serology detects antibodies against SBV, indicating past infection or vaccination. It is indispensable for surveillance, herd immunity assessment, and certification of freedom from infection.

Virus neutralization tests (VNT) are the reference standard for serological diagnosis, offering high specificity and the ability to distinguish SBV from related orthobunyaviruses [20]. However, VNT requires live virus and cell culture facilities, limiting its use to reference laboratories.

Enzyme-linked immunosorbent assays (ELISA) provide a more accessible and higher-throughput alternative. Competitive ELISAs based on the nucleocapsid (N) protein are widely used for screening and show excellent sensitivity and specificity [2,21]. A key limitation is the inability to differentiate vaccination (inactivated vaccines) from natural infection, which complicates surveillance in vaccinated populations—a limitation that has spurred the development of Differentiating Infected from Vaccinated Animals (DIVA)-compatible vaccines and companion serological tests.

Serological differentiation: For DIVA-compatible vaccines (e.g., subunit or deletion mutants), ELISAs targeting the N protein can distinguish vaccinated animals (which lack anti-N antibodies) from naturally infected animals [3]. This approach is critical for maintaining trade and surveillance programs in areas where vaccination is implemented.

4.1.3. Sampling Strategies and Interpretation

A strategic approach to sampling is essential for accurate interpretation:

- Acute infection: Whole blood (EDTA) collected during the febrile phase (2–5 days post-infection) for RT-qPCR; paired serum samples (acute and convalescent, 2–3 weeks apart) for seroconversion.
- Congenital malformations: Fetal brain, spinal cord, and meconium are optimal for RT-qPCR; pre-colostral serum from the newborn (or fetal serum) for IgM detection indicates intrauterine infection.
- Surveillance: Bulk tank milk ELISA is a cost-effective tool for herd-level monitoring in dairy herds [22]; serosurveys in unvaccinated populations provide data on exposure and immunity gaps.

4.2. Vaccine Development: A Progressive Journey

SBV vaccine development has progressed through multiple generations, each addressing limitations of previous platforms while informing *Orthobunyavirus* vaccinology more broadly. Despite technological advances, the commercial withdrawal of licensed vaccines underscores persistent implementation challenges.

4.2.1. First Generation: Inactivated Vaccines

In response to the 2011 epidemic, inactivated whole-virus vaccines were developed within an exceptionally short timeframe. Five candidates evaluated in cattle and sheep prevented or substantially reduced viraemia after challenge; a single immunization proved sufficient to protect sheep, an important practical consideration for extensive production systems [23]. By 2015, three

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inactivated vaccines received marketing authorization in the UK, France, and through the European Union's centralized procedure. However, declining uptake following the initial epidemic led to their withdrawal from the market, leaving livestock industries vulnerable to future resurgence [24].

Limitations: Inactivated vaccines lack DIVA capability, as vaccinated animals seroconvert to all viral proteins, making them serologically indistinguishable from naturally infected animals. This complicates surveillance, certification of freedom from infection, and international trade. Additionally, they often require adjuvants and booster doses, and their production relies on high-containment facilities.

4.2.2. Second Generation: DIVA-Compatible Platforms

The need for DIVA capability drove the development of next-generation vaccines:

- Modified-live deletion mutants: Using reverse genetics, researchers generated SBV mutants lacking NSs, NSm, or both non-structural proteins [23]. A single immunization with the NSs-deletion mutant protected three of four cattle against challenge, while the double-deletion mutant (lacking both NSs and NSm) provided full protection. However, companion diagnostic tests for these candidates remain undeveloped, limiting their practical DIVA application.
- Subunit vaccines: The identification of immunodominant domains on the Gc glycoprotein—particularly the N-terminal head and head-stalk domains—enabled the design of subunit vaccines that induce neutralizing antibody responses [23,25]. Because these vaccines contain only Gc (and not the N protein), vaccinated animals test negative in N-based ELISAs, allowing DIVA differentiation.
- Viral vector and DNA platforms: Replication-competent vectors (e.g., modified vaccinia Ankara) and plasmid DNA encoding protective antigens have been explored experimentally. These platforms offer intrinsic DIVA compatibility and the potential for rapid production, but none have reached commercialization [23].

4.2.3. Emerging Platforms: mRNA and Beyond

mRNA vaccines gained prominence through the COVID-19 pandemic, demonstrating rapid development, scalability, and adaptability [26,27]. These attributes have generated interest in applying mRNA technology to veterinary pathogens such as SBV, where DIVA compatibility and rapid deployment could be advantageous.

Potential benefits: mRNA vaccines are cell-free and can be produced quickly after antigen sequence identification; they can be designed to express only selected antigens (e.g., Gc), enabling DIVA; and platform technologies allow rapid updates to match emerging strains.

Critical considerations:

- Safety in food-producing animals: The safety profile of mRNA vaccines in livestock remains largely unexplored. Human experience has revealed generally acceptable short-term safety, but concerns persist regarding reactogenicity (fever, injection-site inflammation), dose-dependent inflammatory responses, and the lack of long-term data on cellular effects, including persistence of synthetic mRNA or lipid nanoparticle components in tissues [27,28]. In food animals, additional questions arise about tissue residues and food safety.
- Immunological unknowns: Species-specific differences in innate immune sensing, potential for tolerance induction, and durability of protective immunity in ruminants require rigorous evaluation before field deployment.
- Regulatory hurdles: Current veterinary licensing frameworks were designed for conventional vaccine platforms; the novel nature of mRNA constructs poses challenges for standardization, quality control, and post-marketing surveillance [29].
- Commercial sustainability: The withdrawal of earlier SBV vaccines due to low uptake highlights that technological innovation alone does not ensure sustained availability. Commercial viability, farmer acceptance, and integration into existing veterinary infrastructure are equally critical [24].

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Thus, while mRNA platforms offer theoretical advantages for rapid response, their application to SBV must be pursued with rigorous safety evaluation, long-term impact studies, and development of appropriate regulatory pathways.

4.2.4. The Implementation Gap

Despite technological progress, no SBV vaccine is currently marketed in several European countries, leaving livestock industries vulnerable. This implementation gap stems from:

- Commercial disincentives: Endemic diseases with sporadic, unpredictable outbreaks do not generate consistent demand, discouraging manufacturers from maintaining licensed products.
- Regulatory complexity: Maintaining a vaccine license requires ongoing pharmacovigilance and batch-testing, which may not be economically justifiable without sustained sales.
- Farmer perception: The absence of visible clinical disease in many years reduces willingness to vaccinate, particularly in extensive systems where handling animals is costly.

Solutions: Sustaining preparedness requires public-private partnerships, antigen banks, or rapid-deployment platforms (e.g., mRNA or viral vectors) that can be activated when risk increases [24,30]. For SBV, a combination of DIVA-compatible vaccines and companion serological tests would enable targeted vaccination without compromising trade certification.

4.3. Vector Management Strategies

Given the current gaps in vaccination, integrated vector management (IVM) assumes greater importance. IVM combines chemical, ecological, biological, and physical interventions to reduce vector abundance and interrupt virus transmission [13].

- Chemical control: Insecticides (pyrethroids, organophosphates) and repellents can reduce *Culicoides* feeding on livestock. However, practical challenges include cost, labor for repeated application, environmental concerns, and potential for insecticide resistance.
- Ecological management: Reducing or eliminating larval breeding sites (moist organic matter, dung heaps, muddy areas) around livestock facilities can decrease vector populations. Management of manure and drainage is critical.
- Biological control: Research is exploring entomopathogenic fungi, nematodes, and larvivorous organisms, but no biological control product is commercially available for *Culicoides*.
- Physical barriers: Housing animals in insect-proof buildings during peak vector activity periods can prevent exposure. This approach is feasible for intensive dairy or feedlot operations but impractical for extensive pasture-based systems.

Lessons from bluetongue virus: European experience with another *Culicoides*-transmitted pathogen demonstrated that sustained vaccination campaigns are highly effective for disease prevention and even eradication from defined areas [13,23]. IVM alone, while valuable, is insufficient without vaccination in high-risk settings.

4.4. Surveillance and Early Warning Systems

Surveillance is the cornerstone of evidence-based control. Effective surveillance systems integrate:

- Clinical surveillance: Reporting of acute febrile illness in adult ruminants and congenital malformations in newborns. Sentinel herds can provide early indications of virus circulation.
- Entomological surveillance: Monitoring *Culicoides* species composition, abundance, and seasonality. The discovery of winter vector activity in stables [7] highlights the need for year-round surveillance, particularly in indoor environments.
- Serological surveillance: Regular herd-level serosurveys to assess immunity gaps and detect incursions into previously free areas. Bulk tank milk testing offers a cost-effective approach for dairy herds [22].

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- Genomic surveillance: Sequencing of viral isolates or clinical samples enables tracking of strain evolution, reassortment, and introduction pathways [6,19]. NGS can be integrated with routine diagnostic workflows to provide real-time insights.

Early warning systems: In non-endemic regions, early warning systems should integrate meteorological data (temperature, precipitation), vector activity models, and livestock movement patterns to predict high-risk periods and guide preventive measures [14].

4.5. Region-Specific Control Strategies

The epidemiological context dictates the optimal control strategy. Wang et al. [6] emphasize the need to tailor approaches to endemic versus non-endemic regions.

Endemic regions:

- Goal: Minimize clinical impact and economic losses while maintaining trade.
- Strategies:
  - Vaccination of naive replacement stock and breeding animals before first pregnancy, using DIVA-compatible vaccines where available.
  - Integrated vector management to reduce transmission risk.
  - Active surveillance to detect changes in herd immunity or virus circulation.
  - Farmer education on biosecurity and vaccination benefits.

Non-endemic regions:

- Goal: Prevent introduction and ensure rapid detection and response.
- Strategies:
  - Border biosecurity and strict controls on imports of live animals, semen, and embryos from endemic areas.
  - Early warning systems and contingency plans that include access to antigen banks or rapid-deployment vaccine platforms.
  - Sentinel surveillance in high-risk areas (e.g., near ports, livestock assembly points).
  - Public-private partnerships to ensure rapid availability of diagnostics and vaccines in the event of an incursion.

Re-emergence risk: In both settings, climate change and evolving vector ecology can expand the geographic range of SBV, necessitating periodic reassessment of risk maps and control strategies [14,15].

4.6. Diagnostic and Control Challenges: A Summary

Component	Key Tools	Gaps / Challenges
Molecular diagnosis	RT-qPCR, multiplex assays, NGS	Short viremic window; need for standardized protocols; limited capacity in some regions
Serology	VNT, N-based ELISAs	DIVA limitation with inactivated vaccines; need for companion tests for deletion mutants
Vaccines	Inactivated, subunit, modified-live, mRNA (experimental)	Market withdrawal; lack of DIVA for some platforms; regulatory hurdles; commercial sustainability
Vector management	Insecticides, ecological management, physical barriers	Insecticide resistance; cost; limited biological control options; impractical for extensive systems

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Surveillance	Clinical, entomological, serological, genomic	Winter vector activity under-detected; integration of data streams; need for sustained funding

By integrating these diagnostic and control elements, the veterinary community can move from a reactive posture toward a precision-based approach that mitigates the impact of SBV while building capacity to address future arbovirus threats.

5. The Hidden Burden: Economic Impact and Farm-Level Realities

5.1. Quantifying the Cost

The economic impact of SBV varies across production systems and disease scenarios. Using partial budget analysis, Waretszkuta et al. [31] estimated that in a high-impact scenario, losses ranged from €23 to €43 per cow per year and €19 to €37 per ewe per year in France. In a low-impact scenario, losses were approximately half (cattle) or one-third (sheep) of these amounts. These impacts represented 0.6% to 63% of gross margin, illustrating extreme variability in vulnerability.

5.2. A Tale of Two Systems

Economic losses differ fundamentally between production systems. In dairy systems, impacts derive primarily from costs of purchasing and raising replacement heifers, milk production losses during acute infection, and loss of genetic potential from affected offspring. In beef suckler systems, losses are dominated by reduced calf crop value (dead or non-viable calves) and dystocia-related complications affecting cow fertility and survival. Meat sheep systems experience losses from lamb mortality and reduced saleable offspring, while dairy sheep operations combine milk production decreases and unsold replacement lambs [31].

5.3. The UK Experience

A 2025 review of SBV in the United Kingdom noted that the virus can have "catastrophic economic impacts on a farming business through the loss of lambs and adult sheep" [24]. Despite vaccine development in 2018, subsequent withdrawal from the market due to declining uptake has left the UK sheep industry vulnerable, exemplifying the challenge of maintaining control measures for endemic diseases that cause sporadic rather than continuous losses.

6. Comparative Biology: SBV in the Simbu Serogroup Context

6.1. The Simbu Serogroup

SBV belongs to the *Simbu* serogroup within the *Orthobunyavirus* genus, which comprises approximately 25 antigenically distinct viruses. Important veterinary pathogens in this group include *Akabane virus* (Africa, Asia, Australia), *Aino virus*, *Shamonda virus*, and *Shuni virus*. *Oropouche virus*, a human pathogen causing febrile illness in South America, also belongs to this serogroup [5,32]. All *Simbu* serogroup viruses share a tripartite negative-sense RNA genome, transmission by *Culicoides* vectors, and the capacity to cause congenital malformations when naive pregnant ruminants are infected during critical gestational windows.

6.2. Comparative Pathogenesis

Akabane virus has been most extensively studied. In cattle, infections during the final three months of pregnancy result in relatively low disease rates (5–10% of calves affected), while infections during the third and fourth months affect up to 40% of calves; the most severe strains can cause disease in up to 80% of infected animals [5]. In contrast, SBV causes a much lower incidence of

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disease. *Aino* and *Shamonda* viruses produce similar clinical signs, although disease rates are usually much lower unless infection occurs in intensively managed herds with synchronized breeding. *Shuni virus* has been described as a cause of acute encephalitis in horses in Africa, occasional congenital defects in cattle in Israel, and severe fatal encephalitis in calves [33].

6.3. Differential Diagnosis

The clinical and pathological similarities among *Simbu* serogroup infections necessitate laboratory confirmation. Serological testing of pre-colostral offspring samples (for IgM antibodies) and maternal serology provide supportive evidence, while RT-PCR on fetal tissues enables viral detection and differentiation [5,24]. A useful differential feature is that *Akabane virus* does not cause cerebellar lesions, distinguishing it from *Bovine viral diarrhea virus* infection; however, other *Simbu* serogroup viruses appear to produce lesions throughout the brain [5].

7. One Health Perspective

SBV exemplifies the interconnected nature of animal health, environmental change, and socio-economic systems, aligning closely with the One Health framework [34]. Although SBV is not considered zoonotic, its emergence and persistence are driven by ecological and climatic factors that also influence other vector-borne pathogens of human and veterinary importance.

From an environmental perspective, climate change has altered the distribution, abundance, and seasonal activity of *Culicoides* vectors. Warmer temperatures and modified precipitation patterns have expanded suitable habitats and extended transmission periods, facilitating viral persistence in regions previously considered low-risk [14,15]. These same environmental drivers are implicated in the emergence of other arboviruses, highlighting SBV as a sentinel indicator of broader ecological shifts.

From an animal health standpoint, SBV continues to impact livestock productivity, welfare, and reproductive performance. The disease underscores the vulnerability of intensive and extensive production systems to vector-borne infections and highlights the importance of integrating surveillance, vaccination, and vector control strategies [6,34].

Economically, SBV outbreaks have significant consequences for farmers, affecting income stability and farm sustainability. Indirect impacts include trade restrictions and increased costs associated with disease management and prevention. These economic pressures influence decision-making regarding vaccination uptake and biosecurity measures, creating feedback loops that affect disease dynamics [31].

At the interface of wildlife and livestock, the potential role of wild ruminants in maintaining SBV circulation remains unclear. Seropositivity has been detected in various wild ruminant species [35], but their contribution to viral perpetuation and spatial spread is unknown. Wildlife reservoirs could complicate eradication efforts and provide a source for re-infection of livestock after control measures cease.

Finally, SBV highlights the importance of interdisciplinary collaboration among veterinarians, entomologists, climatologists, and policymakers. Effective management requires coordinated approaches that integrate data on vector ecology, climate trends, animal health, and socio-economic factors [6,34].

8. Future Perspectives and Unresolved Questions

8.1. The Endemic Reality

Fifteen years after its emergence, SBV is firmly established as an endemic pathogen across Europe, with a pattern of wave-like re-emergence driven by waning herd immunity and annual vector activity. The critical unanswered question is what trajectory this endemicity will follow. The answer depends on multiple factors: the duration of protective immunity (natural and vaccine-

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induced), transmission efficiency in different production systems, and the impact of climate change on vector populations and seasonal activity patterns [3,6].

8.2. The Challenge of Vaccine Availability

The withdrawal of SBV vaccines from some European markets due to low uptake presents a critical vulnerability. Should a major resurgence occur—perhaps driven by favorable vector conditions or introduction into a naive population—the livestock industry would again face an epidemic without ready access to effective countermeasures. This situation argues for maintaining vaccine banks or rapid-deployment platforms that can be activated quickly when needed [6,26].

8.3. Climate Change and Vector Distribution

The evidence for winter activity of *Culicoides* vectors inside livestock buildings fundamentally challenges previous assumptions about transmission seasonality [7]. If continuous, low-level transmission can occur year-round in protected microenvironments, the concept of a vector-free period—and trade restrictions based on it—requires re-evaluation. Further research is urgently needed to quantify the extent to which winter midge activity actually drives virus transmission.

8.4. Wildlife and Silent Maintenance

The role of wildlife in maintaining SBV transmission cycles remains poorly characterized. Seropositivity in wild ruminants has been documented [35], but their contribution to viral perpetuation and spatial spread is unknown. If wildlife reservoirs exist, they could complicate eradication efforts and provide a source for re-infection of livestock after control measures cease. This represents a key research priority within a One Health context.

8.5. Genomic Surveillance and Emerging Strains

The identification by Varela et al. [10] of a biological SBV clone that displayed increased virulence in mice after cell culture passage raises the possibility that SBV could evolve towards enhanced pathogenicity. Genomic surveillance programs are needed to monitor viral evolution, detect antigenic drift that might compromise vaccine efficacy, and identify emergence of strains with altered tropism or virulence [3,6].

8.6. Application to Future Arbovirus Emergences

The SBV experience provides a template for responding to future arbovirus emergences. The rapid development of reverse genetics systems, the identification of immunodominant domains for subunit vaccine design, and the application of multiplex diagnostic platforms all represent advances that can be deployed against future threats. Investment in platform technologies and fundamental research pays dividends when novel pathogens appear [6,8].

9. Conclusions

Schmallenberg virus is far from a "solved" problem. It has become a model pathogen for understanding the interplay between viral pathogenesis, climate-driven vector ecology, livestock production systems, and the application of modern biotechnology to disease control. The tools developed over the past fifteen years—from reverse genetics to DIVA-compatible vaccines to multiplex diagnostics—have positioned the veterinary community to respond more effectively not only to SBV but to the next emerging arbovirus. However, critical gaps remain: the withdrawal of vaccines from some markets, the evidence for winter vector activity challenging established transmission models, and the unknown role of wildlife in viral maintenance all demand continued research investment. As climate change continues to alter vector distribution and seasonal activity patterns, SBV serves as both a sentinel of environmental change and a test case for our capacity to

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manage emerging infectious diseases in an interconnected world. Sustained investment in surveillance, vaccine platforms, and interdisciplinary research remains essential.

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Abbreviations

The following abbreviations are used in this manuscript:

SBV	*Schmallenberg virus*
N	nucleocapsid protein
NSs	non-structural protein
IFN	interferon
SBVΔNSs	deletion mutant lacking NSs
NGS	Next-generation sequencing
VNT	Virus neutralization tests
ELISA	Enzyme-linked immunosorbent assays
DIVA	Differentiating Infected from Vaccinated Animals
IVM	integrated vector management

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