

# Maximising Impact, Optimising Investment



## ↗ Cost-Effective Strategies for Leishmaniasis Prevention



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Landscape of the Sea of Galilee region (Israel), an area where environmental conditions, human building activity, and reservoir–vector interactions contribute to the transmission dynamics of zoonotic leishmaniasis.

**L**eishmaniasis is an endemic vector-borne disease in Europe and Mediterranean countries, spread by Phlebotomine sand flies, with a risk of local outbreaks and geographic expansion [1–3].

Visceral leishmaniasis (VL) is more likely to be detected due to hospitalization requirements, whereas human cutaneous leishmaniasis (CL) and canine leishmaniasis (CanL) remain substantially underreported. As a result, the overall burden of leishmaniasis is heavily underestimated [4]. In Europe and Mediterranean countries, CL probably affects thousands of people every year despite limited detection [5,6].

The same species of *Leishmania* parasite may cause different clinical outcomes, depending on the host's immune response and the intensity of transmission [7]. Transmission is highly localised and influenced by climate variability, environmental change, and human–animal–vector interactions [8,9]. This raises a critical policy challenge: how to allocate resources efficiently in a context where risk is uneven, dynamic, and often underreported.

To inform decision-making, the CLIMOS project conducted a multi-country cost-effectiveness analysis (CEA) of major preventive interventions across 18 European and Mediterranean countries. The analysis compared a no-intervention scenario

with scenarios in which dog vaccination, insecticide-treated dog collars, or vector control measures were implemented on a large scale.

The CEA suggests that the widespread implementation of these interventions is generally not cost-effective in areas with low transmission (where clinical case numbers are relatively low). However, national-level estimates may mask local transmission, as leishmaniasis risk is often concentrated in specific geographic areas. This suggests that the cost-effectiveness of interventions depends strongly on how and where they are applied, with greater impact achieved in targeting areas with a higher risk of transmission and a strong integrated surveillance system.

The analysis also highlights substantial uncertainty in both the true disease burden and the effectiveness of interventions, emphasizing the need for mandatory notification in both the human and animal health sectors to improve burden estimation. Accurate case incidence data are required to power evaluation studies to help identify and remediate uncertainties in the effectiveness of interventions.

These efforts should be supported by efficient reporting systems, real-time data analysis, and rapid response capacity to detect and mitigate emerging transmission.

## Key messages for decision-makers

- **Mandatory notification of human and canine leishmaniasis should be established across sectors.**
- **Transition from uniform national strategies to targeted, data-driven, informed risk-based interventions.**
- **Strengthen integrated surveillance systems to enable timely detection, analysis, and response.**
- **Prioritise cost-effective measures, such as insecticide-impregnated dog collars, in endemic settings.**
- **Build a stronger evidence-based approach, including studies on the intervention effectiveness in endemic contexts.**
- **Promote the development and use of tools such as the CLIMOS toolkit together with WHO operational manuals on leishmaniasis vector control and surveillance [10], to inform data-driven decision-making.**

## 1.1 A Changing Epidemiological Landscape

Leishmaniasis is no longer confined to traditionally endemic regions. Across Europe and the Mediterranean, climate change, altered precipitation patterns, changes in land use, urban expansion, and increased human and animal mobility contribute to the expansion of suitable habitats for sand fly vectors and reservoir hosts, reshaping the transmission of sand fly-borne disease [9,11]. While these changes are often gradual and difficult to detect, they can lead to persistent transmission cycles with significant public health implications.

Leishmaniasis in Europe is characterized by strong spatial heterogeneity, with transmission concentrated in localised foci shaped by ecological, environmental, and socio-economic conditions. Consequently, areas that appear low-risk at a macro level may contain high-risk pockets capable of sustaining transmission and triggering outbreaks [1,9].

## 1.2 - The Policy Challenge: Data Gaps and System Complexity

The apparent low incidence of sand fly-borne diseases (SFBDs), including leishmaniasis and sand fly-borne phleboviruses, in most European countries, is largely driven by underreporting and incomplete surveillance [10,12]. This creates a complex challenge for policymakers. On one hand, the true disease burden is not accurately captured, and, when aggregated at a macro level, it may appear insufficient to justify large-scale investment in prevention and control. However, on the other hand, the consequences of local transmission, including severe clinical outcomes, healthcare costs, and potential geographic expansion, can be significant [13,14].

Furthermore, leishmaniasis poses a significant One Health challenge [15]. In Europe, zoonotic visceral leishmaniasis caused by *Leishmania infantum* is particularly associated with domestic dogs as the main reservoir host [16,17]. Effective control therefore, requires coordinated action across sectors, including public health, veterinary services, environmental management, and local authorities.

While the CLIMOS analysis focuses only on leishmaniasis, it is important to highlight that there are currently no cost-benefit analyses for phlebovirus interventions. This underscores the need for future research within integrated sand fly-borne disease frameworks.

## 1.3 - Gaps in Economic Evidence and Decision Support

The biological and ecological aspects of leishmaniasis are well understood; however, there is limited economic evidence to inform policy decisions in Europe and worldwide [12].

Most available economic evaluation studies focus on isolated components of transmission and are conducted in high-burden settings. They often rely on proxy outcomes, such as infection in vectors or reservoirs, rather than human clinical outcomes [10,18]. These studies also lack robust evaluation designs, such as cluster randomized controlled trials (CRCTs) or other rigorous field-based evaluations. Similarly, vector control faces a comparable challenge: although new tools are being developed, their implementation remains constrained by a lack of evidence regarding their effectiveness in preventing infection and disease and their relative cost-effectiveness [10]. As a result, considerable uncertainty exists when translating expert recommendations into policy and practice, particularly when deciding which interventions to prioritise, where to implement them, and whether investments in low- to moderate-risk settings are justified. Nevertheless, these settings may still require preparedness capacity for rapid response in the event of localised outbreaks or sudden increases in transmission [13,14].

**These limitations highlight the need for a more strategic, risk-based, and economically informed approach to preventing leishmaniasis, which is supported by data and decision-support tools.**

## 2. CLIMOS Cost-effectiveness Analysis

The cost-effectiveness and economic performance of leishmaniasis interventions vary depending on how and where they are implemented.

The CLIMOS project conducted a multi-country CEA covering 18 European and Mediterranean countries, evaluating the cost-effectiveness of key preventive interventions targeting zoonotic leishmaniasis.

Key intervention strategies were compared with a counterfactual scenario of no intervention, using standard public health metrics, including cost per disability-adjusted life year (DALY) averted, net economic welfare gain, and net productivity gain. Due to the limited availability of data, the analysis was based on the combination of published evidence, expert inputs, and proxy indicators such

### 2.1. Key Findings from the Analysis

The CEA suggests that interventions may be more economically justifiable when focused on higher-risk areas or during periods of increased transmission compared to low-to-medium risk areas. Nevertheless, their cost-effectiveness is influenced by the degree of coverage required and achieved, householder compliance, transmission intensity, disease incidence, and the local ecological and epidemiological context.

Preventive interventions evaluated in the CEA included insecticide-impregnated dog collars, dog vaccinations, indoor residual spraying (IRS), and long-lasting insecticidal nets (LLINs). Insecticide-impregnated dog collars generally showed comparatively better cost-effectiveness in zoonotic *Leishmania infantum* settings,

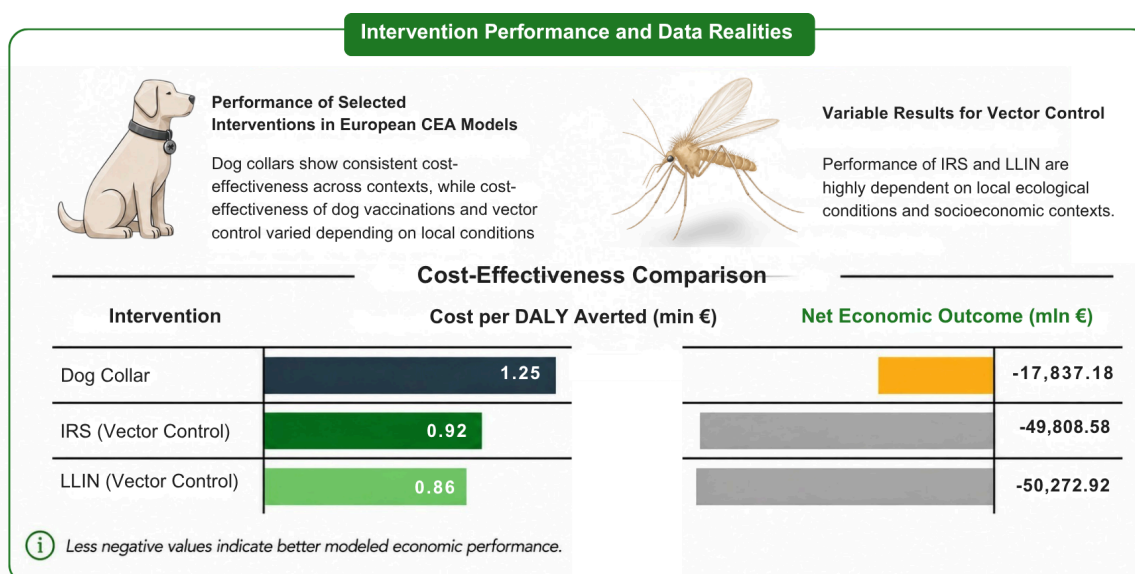
as reductions in infection rather than clinical data.

Although CEAs of leishmaniasis preventive interventions with human-centric outcomes remain scarce on a global scale, this CEA is one of the first structured attempts to assess the cost-effectiveness of leishmaniasis prevention in a European context. However, data limitations, including the scarcity of CRCTs, limited data on human-centred outcomes, and variability across settings, introduce uncertainty.

Nevertheless, this analysis aims to explore the public health and economic implications under real-world conditions. Rather than providing precise estimates, the analysis identifies general relative patterns to support more informed, risk-based decision-making.

particularly when implemented in higher-risk areas and with sufficient coverage and compliance. Vector control measures, including IRS and LLINs, showed more variable cost-effectiveness across settings. While these interventions may contribute to reducing transmission, their effectiveness depends strongly on local ecological conditions, operational feasibility, and human and vector behaviours. For example, IRS and LLINs are designed primarily for indoor applications, whereas some sand fly vector species prefer to bite predominantly outside. Furthermore, the high cost of large-scale implementation can limit their value for health in many European contexts.

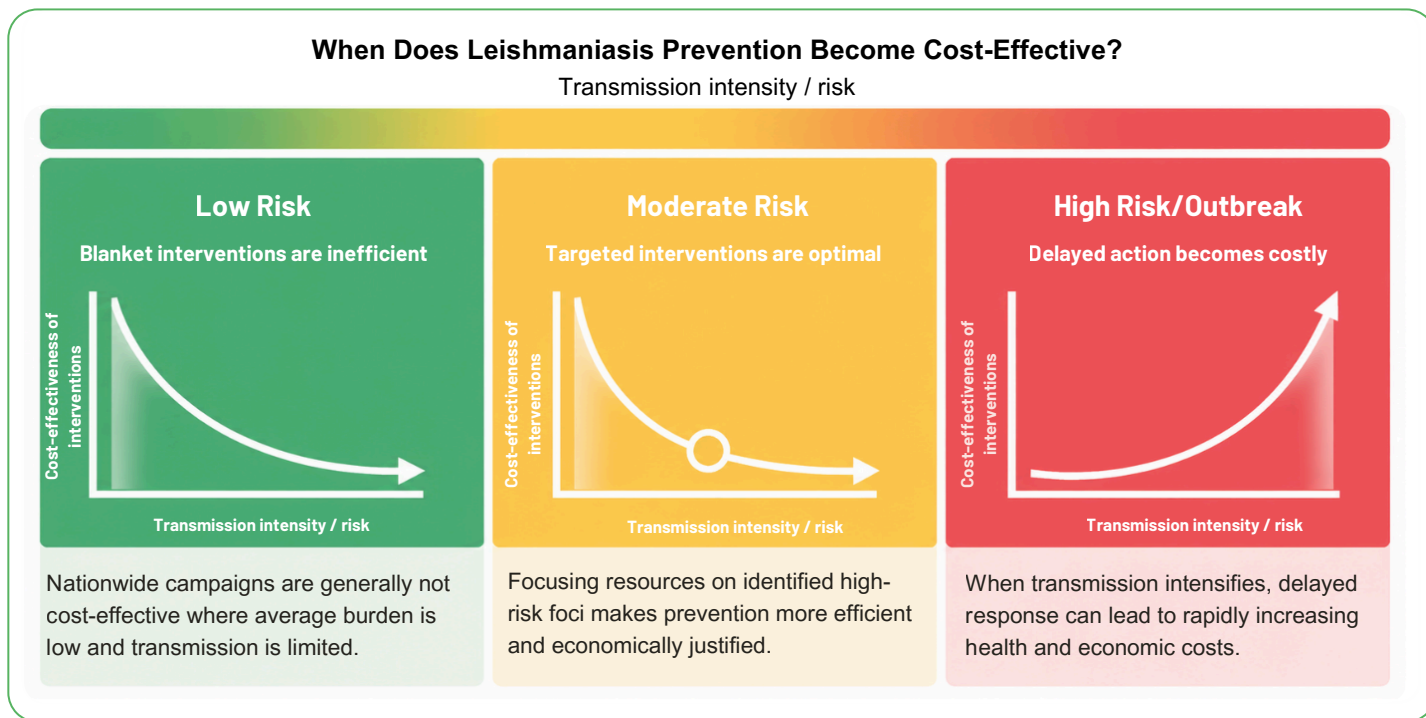
The comparative performance of selected interventions across European CEA models is shown in Figure 1.



**Figure 1:** Comparative economic performance of selected interventions across European CEA models. Lower cost per DALY averted, and less negative economic outcomes indicate comparatively better modelled performance. Results are model-based and context-dependent.

# 3. Interpretation for Policy

Building on these findings, the CEA highlights a key policy message: the effectiveness of leishmaniasis prevention and control measures depends on how well interventions are aligned with the distribution of risk (Figure 2).



**Figure 2:** Conceptual illustration on how the relative cost-effectiveness of prevention strategies changes according to transmission risk and outbreak intensity.

**The cost-effectiveness of leishmaniasis prevention varies according to the level of risk: blanket approaches perform poorly in areas of low risk, targeted interventions are most efficient in identified hotspots, and the cost of delayed action increases during outbreaks.**

The results support a policy shift towards targeted, risk-informed strategies, where interventions are deployed selectively based on entomological and epidemiological evidence requiring surveillance systems, rather than on administrative boundaries.

A key implication of this shift is the central role of active surveillance, supported by mandatory notification (covering both human and animal cases), efficient reporting, and rapid response systems. In endemic settings, the analysis of hospital-reported visceral leishmaniasis cases may help identify areas requiring intensified surveillance and targeted interventions. In this sense, surveillance should not be viewed as a supporting activity but as a core component of cost-effective prevention. By enabling the timely identification of high-risk areas and emerging transmission, integrated surveillance systems that combine human, animal, and vector data are central to targeted intervention strategies.

At the same time, a defining feature of the CLIMOS analysis is the uncertainty associated with both disease burden and intervention effectiveness.

Rather than delaying action, this supports the adoption of flexible, adaptive strategies that can operate under incomplete information.

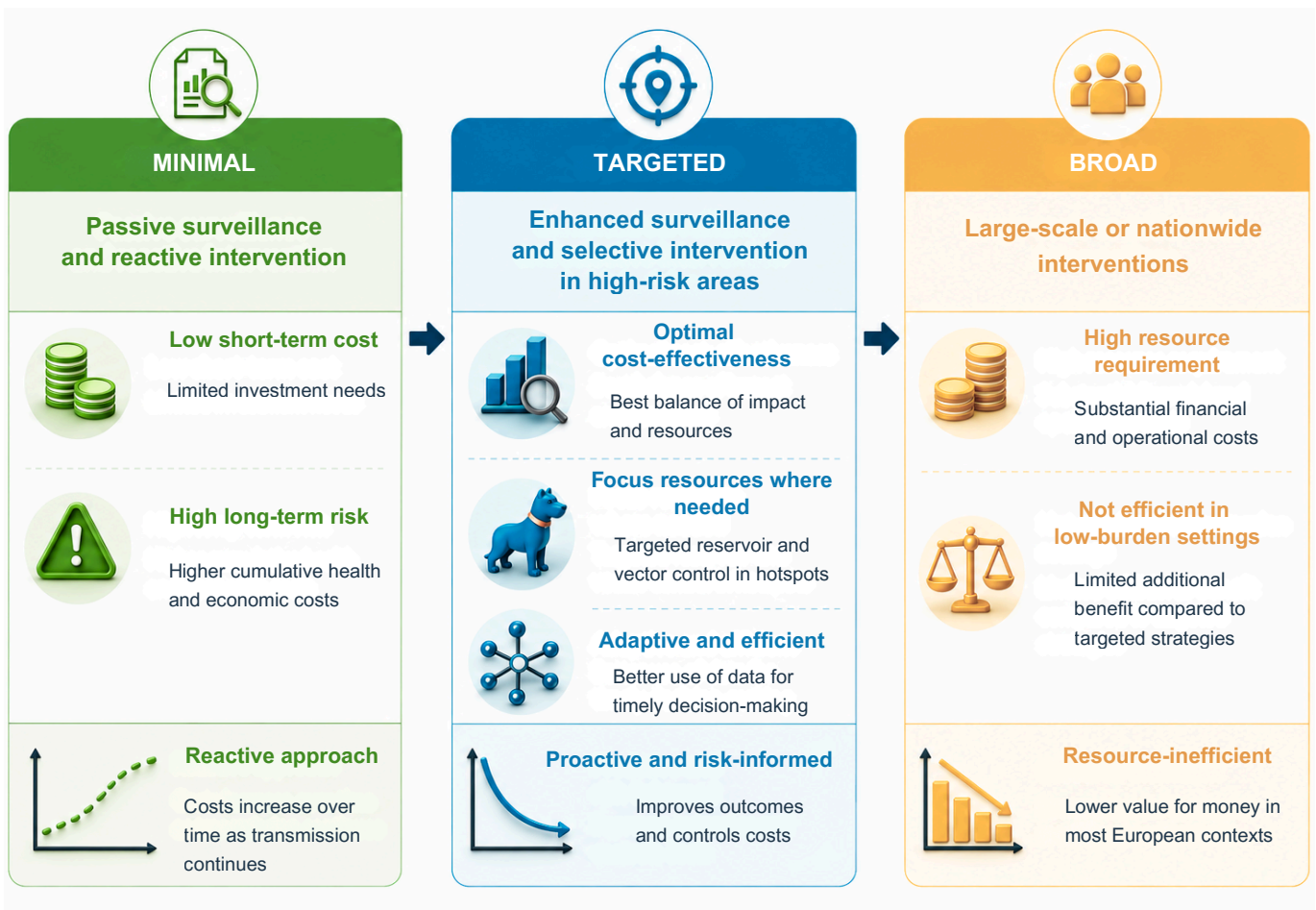
Failure to act early may allow localised transmission to spread, increasing long-term public health and economic costs. Taking early, targeted action can limit this expansion and reduce the need for more complex resource-intensive responses. Likewise, post-intervention sustained monitoring is the key to certify elimination as a public health problem.

Taken together, these findings suggest a shift in how leishmaniasis prevention is conceptualized and implemented in Europe. The key issue is not whether interventions are cost-effective, but whether health systems are equipped to deploy them strategically.

This requires moving from static, one-size-fits-all approaches towards dynamic, risk-informed frameworks that integrate surveillance, targeted intervention, and early warning systems. Within this paradigm, economic analysis becomes a tool for optimizing decisions rather than restricting action.

## 4. Policy Options and Strategic Pathways

The findings of the CLIMOS CEA do not identify a single, universal solution. Instead, it highlights a range of strategic pathways that differ in terms of their level of ambition, resource requirements, and expected outcomes. In this context, tools that support real-time risk assessment and adaptive planning are essential for implementation. The CLIMOS framework provides this capability, enabling a more efficient allocation of resources and supporting a shift from reactive to anticipatory public health strategies (Figure 3).



**Figure 3:** Three strategic pathways for Leishmaniasis prevention and control

Overall, the evidence suggests that targeted, surveillance-informed strategies are the most balanced and effective approach to preventing leishmaniasis in Europe.

# 5. Key Recommendations

The following actions translate the CLIMOS framework into practical priorities for implementation (Figure 4):

**Surveillance:** Ensure the efficient, mandatory notification of human and animal leishmaniasis cases, and strengthen integrated and sustainable surveillance systems. This is essential for improving the accuracy of disease burden estimates and enabling the timely detection of transmission across human, animal, and vector systems.

**Targeting:** Interventions should be implemented in a targeted and adaptive manner. Resources should be directed towards areas where transmission is established or emerging, using risk-based criteria rather than administrative boundaries.

**Interventions:** Insecticide-impregnated dog collars may represent a useful preventive option in zoonotic *Leishmania infantum* endemic settings when implemented with sufficient coverage, compliance, and sustained replacement. Their use should be considered alongside local epidemiological conditions, operational feasibility, and integrated surveillance data.

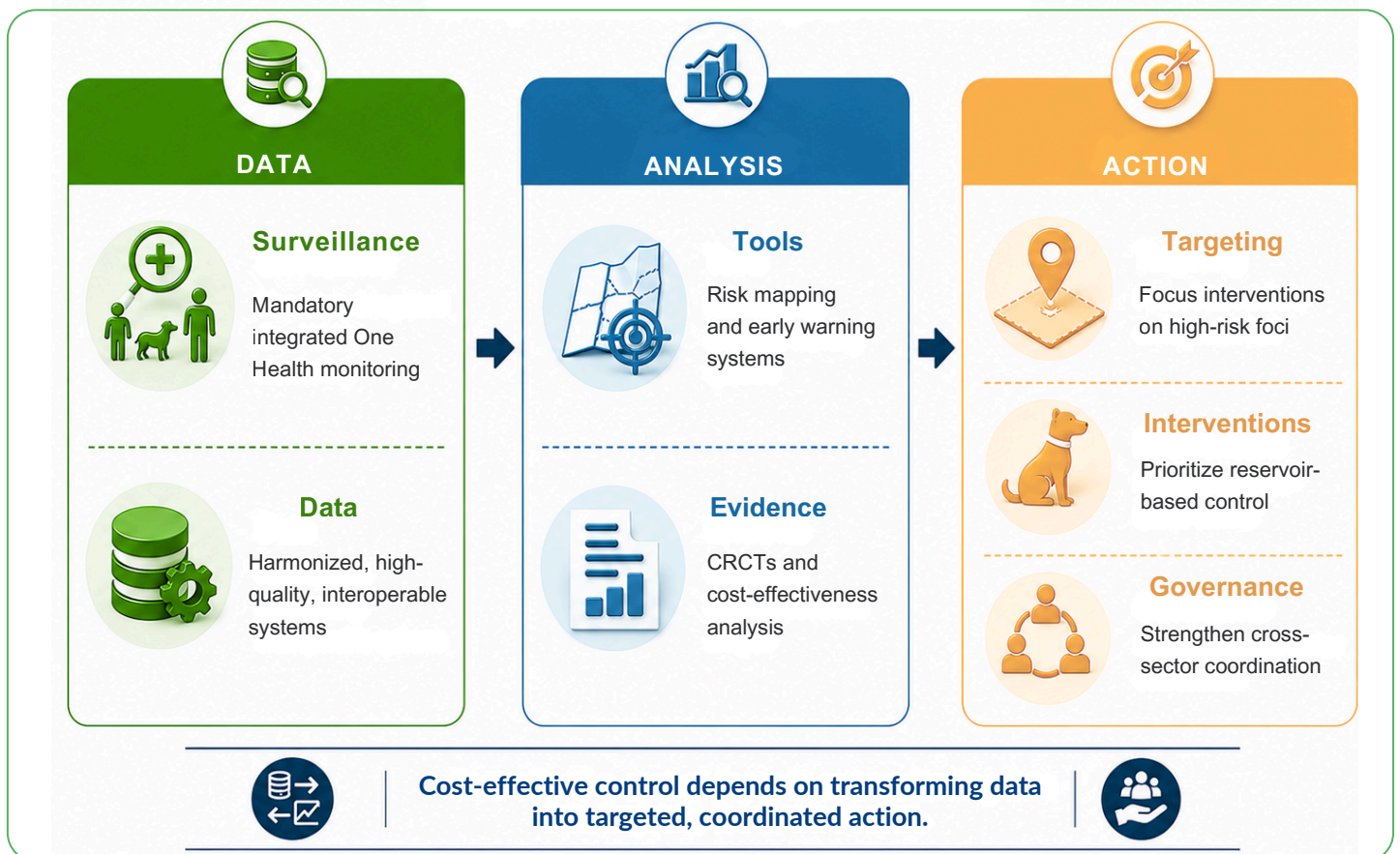
**Evidence:** At the same time, there is a clear need to improve the quality of evidence used for decision-making purposes. Policymakers should support the development of high-quality studies, including CRCTs, operational evaluations, and CEA.

**Data:** Improving the quality and availability of data is essential. This includes improving the availability of long-term time-series data. Efforts should focus on harmonizing indicators, improving data completeness and comparability, and strengthening integration across human, animal, and environmental systems.

**Tools:** Integrating the tools developed within the CLIMOS project, including early warning systems and risk assessment tools, can help identify high-risk areas and allocate resources more efficiently.

**Governance:** Effective implementation requires strong cross-sector and even cross-border coordination. Collaboration between human health, veterinary, environmental, and local authorities must be strengthened to ensure surveillance data is translated into timely, coordinated actions.

**Figure 4:** From Data to Action: A Strategic Framework for Cost-Effective Leishmaniasis Control. Turning surveillance into targeted intervention



# 6. The CLIMOS Contribution

The CLIMOS CEA highlights a critical limitation of leishmaniasis policy in Europe: the scarcity of data based on human health outcomes, particularly in areas with low- to moderate disease prevalence, means that decisions are often based on indirect indicators, such as the presence of vectors and canine reservoirs and their infections, or on data generated in regions with higher disease prevalence and different transmission components that may not be fully applicable to the European context.

Well-designed studies are needed, including operational evaluations, CRCTs where feasible, and alternative approaches based on markers of human exposure or infection, particularly in low-incidence European settings where clinical outcomes alone may be insufficient to power large-scale studies. In addition, there is a limited understanding of how intervention effectiveness varies across ecological, operational, and socio-economic contexts.

Uncertainty in disease burden remains a major challenge. Underreporting of human cases, differences in diagnostic practises and test accuracies, and incomplete surveillance of infected and infectious vectors and animal reservoirs lead to an incomplete picture of the risk of transmission.

Addressing these limitations requires a shift towards integrated, risk-informed surveillance and decision-making approaches that can operate within the complexities of the real world (Figure 5).



Figure 5: The CLIMOS Framework for Cost-Effective Leishmaniasis Prevention

The CLIMOS project responds to the challenges associated with limited human health outcome data by providing an integrated framework for risk-informed decision-making. By combining climate, environmental, vector, and available epidemiological data, CLIMOS enables the creation of risk assessments that are both spatially explicit and temporally dynamic for leishmaniasis and potentially other sand fly-borne diseases. This supports the identification of areas where interventions are likely to be most cost-effective.

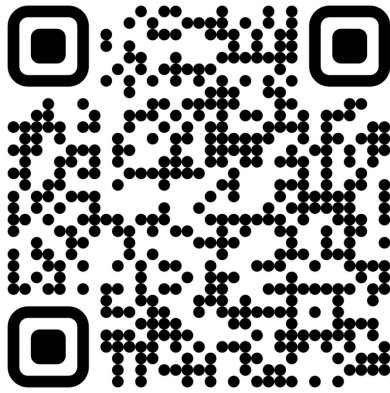
**CLIMOS** functions as both a research initiative and a decision-support system, enabling more efficient, evidence-based public health action.

Ultimately, the evidence is clear: the question is no longer whether prevention is economically justified, but rather how, where, when, and at what scale to intervene.

**Effective and efficient control does not depend on doing more; it depends on doing better by targeting the right interventions in the right places at the right time.**

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