Risk-assessment of *Aedes*-borne diseases and need for modelling-tools for decision making

- Olivier Briët

- Climate-Sensitive Vector Dynamics Modelling Workshop
- 19–20 September 2024, Bologna, Italy

Abstract

- With *Aedes albopictus* spreading in Europe, and outbreaks of Aedes-borne diseases occurring with increasing frequency, there is increasing need for tools to estimate the risk of these diseases, as well as for informing public health control strategies. This talk discusses statistical and mathematical modelling approaches for risk assessment and scenario modelling, including data needs on cost-effectiveness of interventions.

Risk assessment questions

- probability of transmission (in the EU)
- Risk = X
- impact (severity and amount of disease)
- Modified from https://www.ecdc.europa.eu/sites/default/files/documents/operational-tool-rapid-risk-assessment-methodolgy-ecdc-2019.pdf

- What is the current/future probability of an outbreak happening in a geographic area?
- What is the expected size of an outbreak, if it occurs? (we do not yet look at impact in terms of e.g. DHF)
- How could the public health response (vector control/case finding) mitigate the probability and impact?

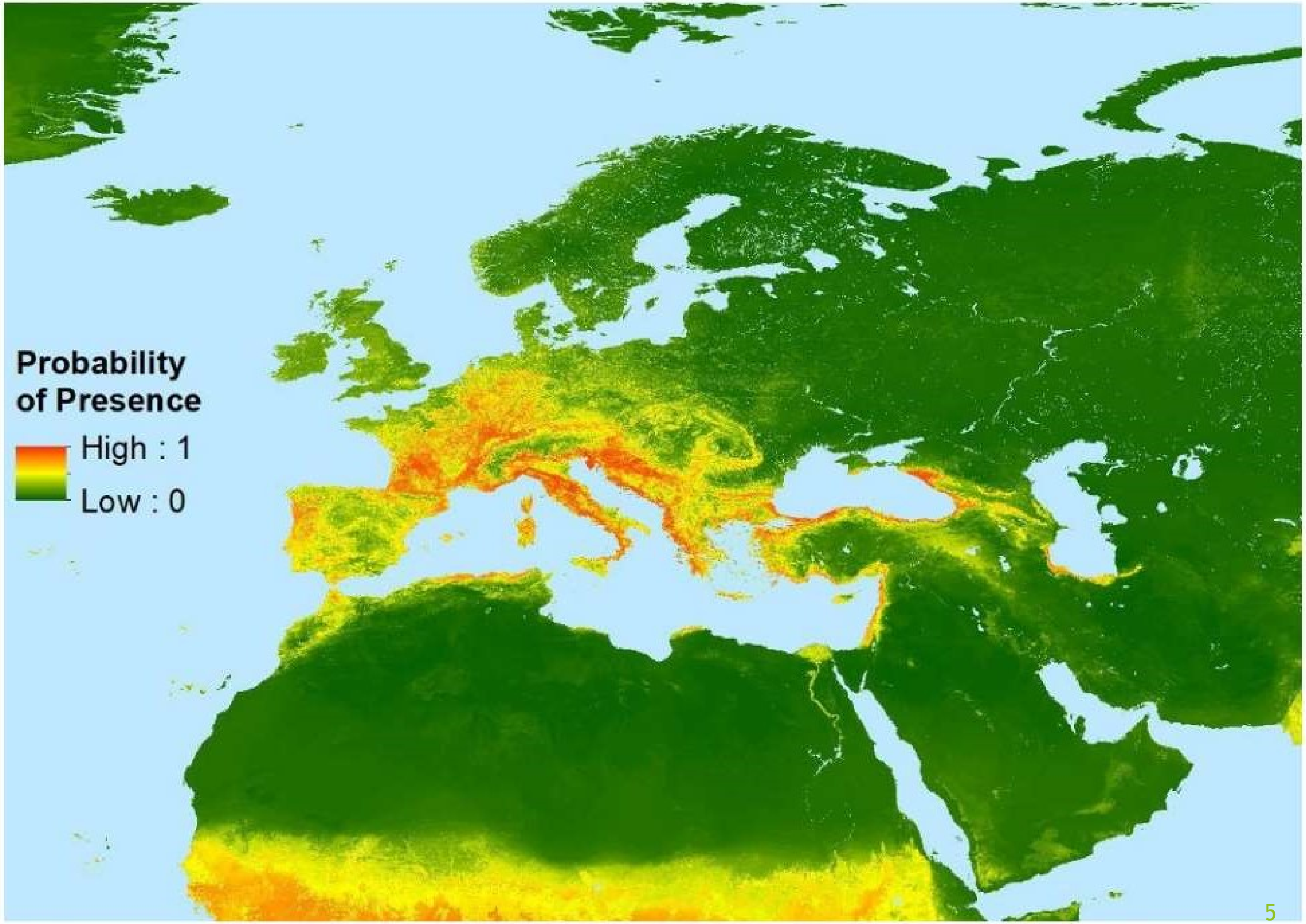
Statistical and mathematical modelling

- **Where vectors are not present:**
- Are the environmental and climatic conditions appropriate for the establishment of competent vectors in a particular area?
- Model ecological niche suitability of the area

RVF vector distribution models

VectorNet European Network for Medical and Veterinary Entomology

Wint et al., 2020 doi: 10.2903/sp.efsa.2020.EN-1800



Masked predictions for *Ae. albopictus.*

Wint et al., 2020 doi:10.2903/sp.efsa.2020.EN-1847

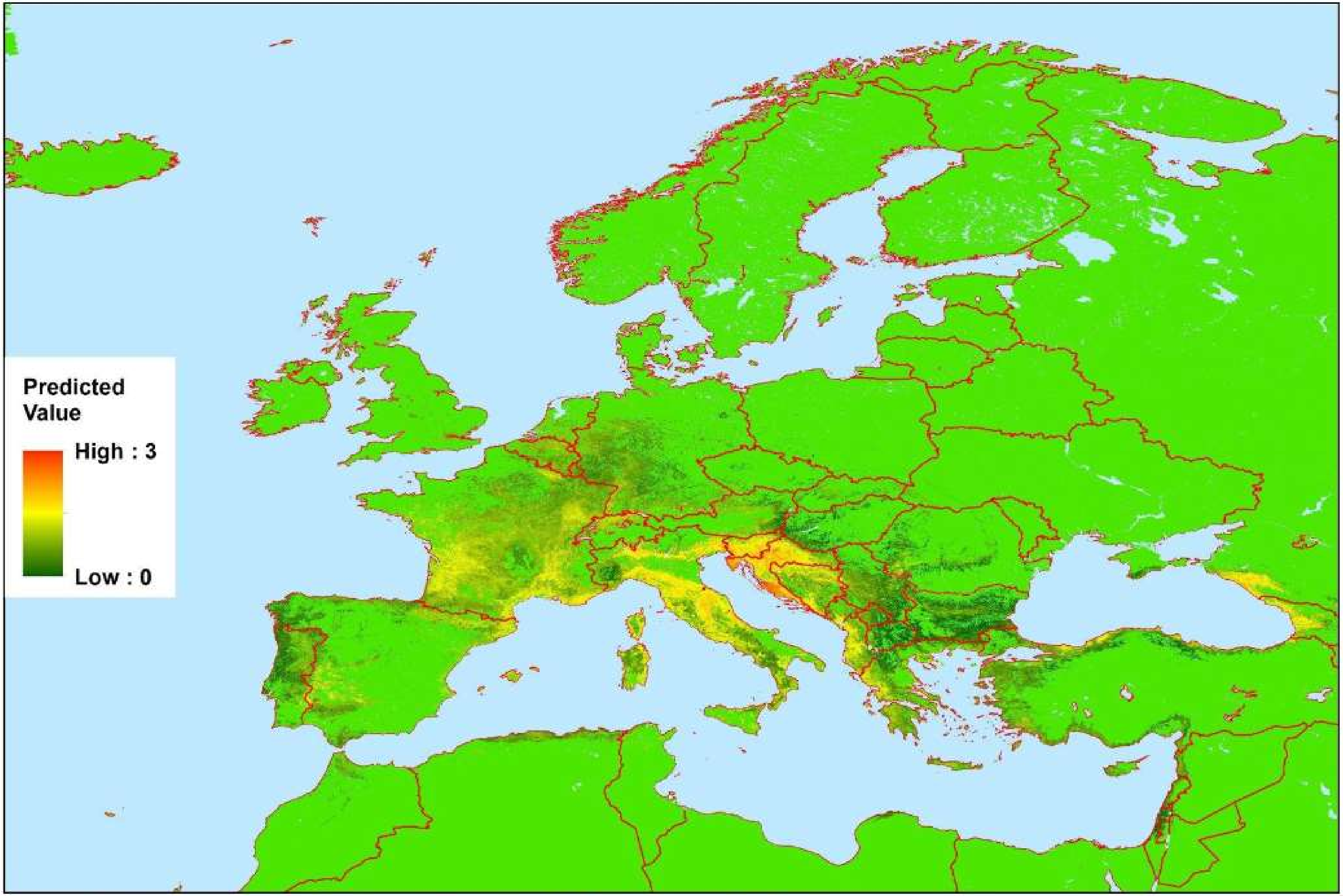


Figure 3: Predicted abundance (log egg equivalent), masked, 1 km aggregation for *Aedes albopictus*.

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Statistical and mathematical modelling

- **Where vectors are not present**:
  - Are the environmental and climatic conditions appropriate for the establishment of competent vectors in a particular area?
  - Model ecological niche suitability of the area

- **Where vectors are present**:
  - What is the receptivity of the vectors in an area and at a timepoint to transmit the disease in case of importation?
  - Model the vectorial capacity (number of expected onward transmissions if an infectious individual is exposed to the vector population for one day) of the vectors in an area at a given time.
  - What is the vulnerability (rate of importation of viraemic individuals)?
  - Statistical prediction models of imported cases in space and time dependent on travel data and prevalence/incidence in source countries.
  - What is the receptivity in terms of capacity of the health system to reduce exposure of mosquitoes to imported cases
  - Model controlled reproduction number (Rc) based on duration of infection (and case-detection-action delays)

Statistical and mathematical modelling (continued)

- **Where local transmission is likely, and depending on the past and future weather conditions:**

- What is the expected size of an outbreak, if it occurs?

- Model Rc based on health system response (including preventive vector control)

- What are the most effective and cost-effective (accepted) public-health strategies for mitigating the probability and impact of local transmission?

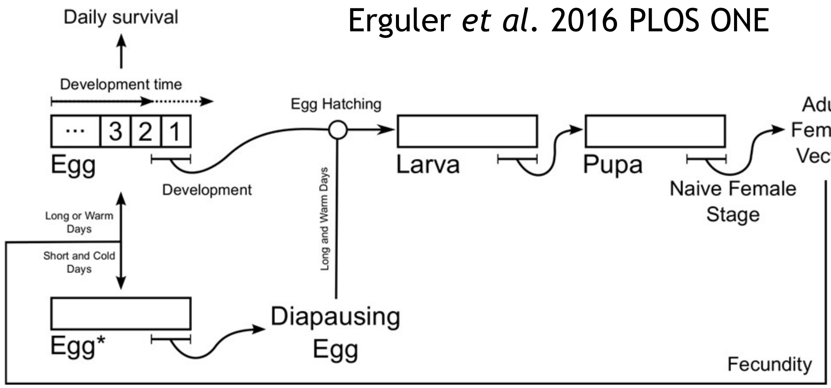
- Scenario-modelling combined with intervention cost-effectiveness data

Risk modelling at ECDC

- ArboRisk – a tool in development to provide ‘near-real time’ maps of risk at NUTS3 spatial resolution and weekly temporal resolution in terms of:
  - Outbreak risk (autochthonous transmission happening)
  - Outbreak impact (the size of a possible outbreak)

- Using:
  - Virus importation probability, based on:
    - Historically imported cases
    - Human population density
    - Distance to airports
    - IATA passenger data
  - Vector dynamic model, based on:
    - Vector presence
    - Rainfall
    - Temperature
    - Photoperiod
    - Human population density
  - Dynamic transmission model, based on:
    - Temperature
    - Vector model
    - Virus importation
    - Autochthonous transmission data for scaling of results

Erguler *et al*. 2016 PLOS ONE

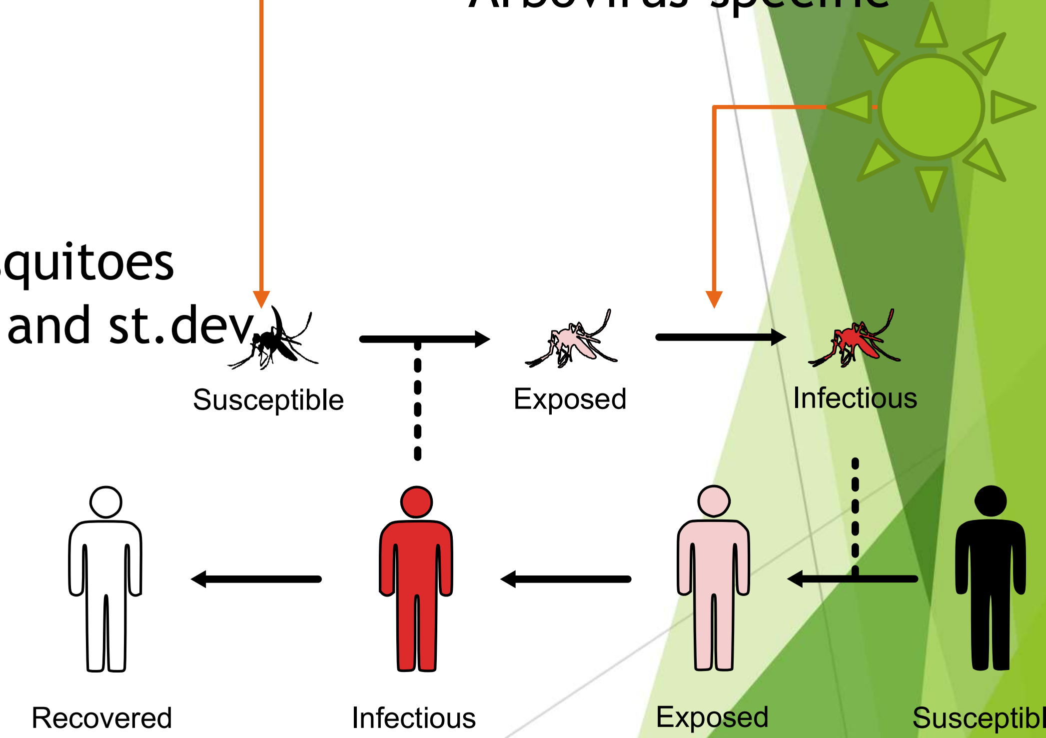


Extrinsic incubation period (EIP)

- Temperature-driven
- Arbovirus-specific

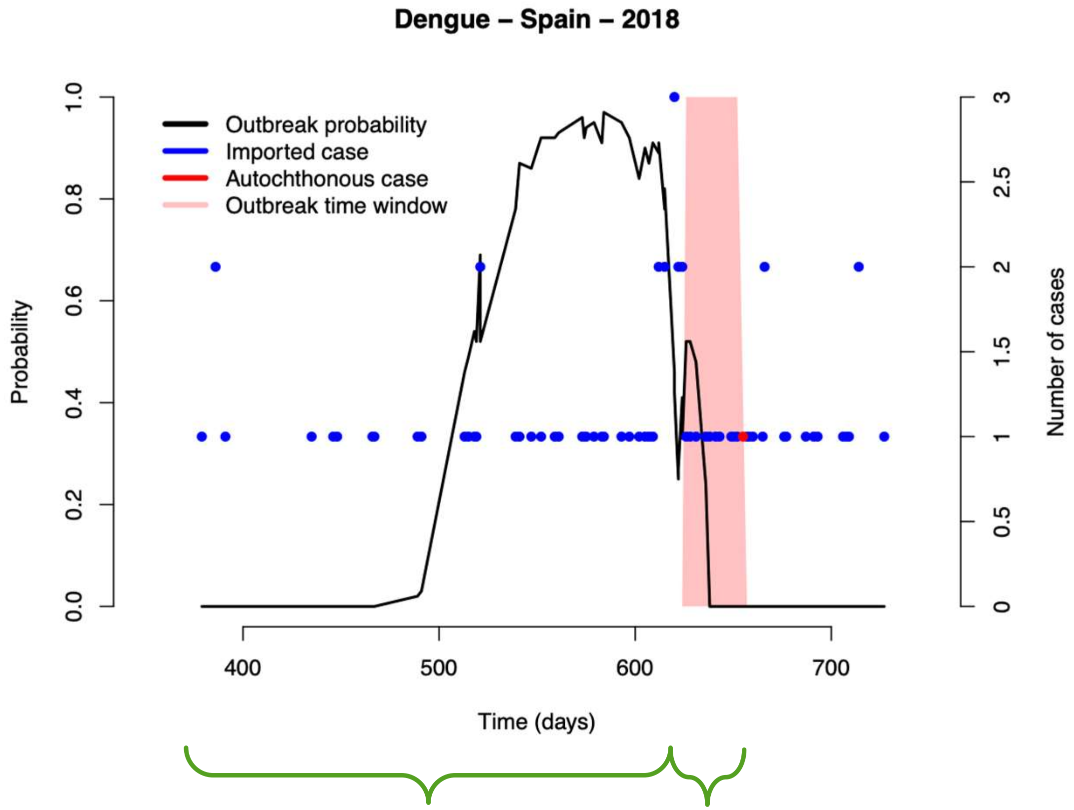
Transmission model input

- (Relative) number of adult female mosquitoes
- Adult female mosquito lifetime (mean and st.dev.)
- Fecundity
- Mean air temperature



Modification from Erguler *et al*. 2017 PLOS ONE

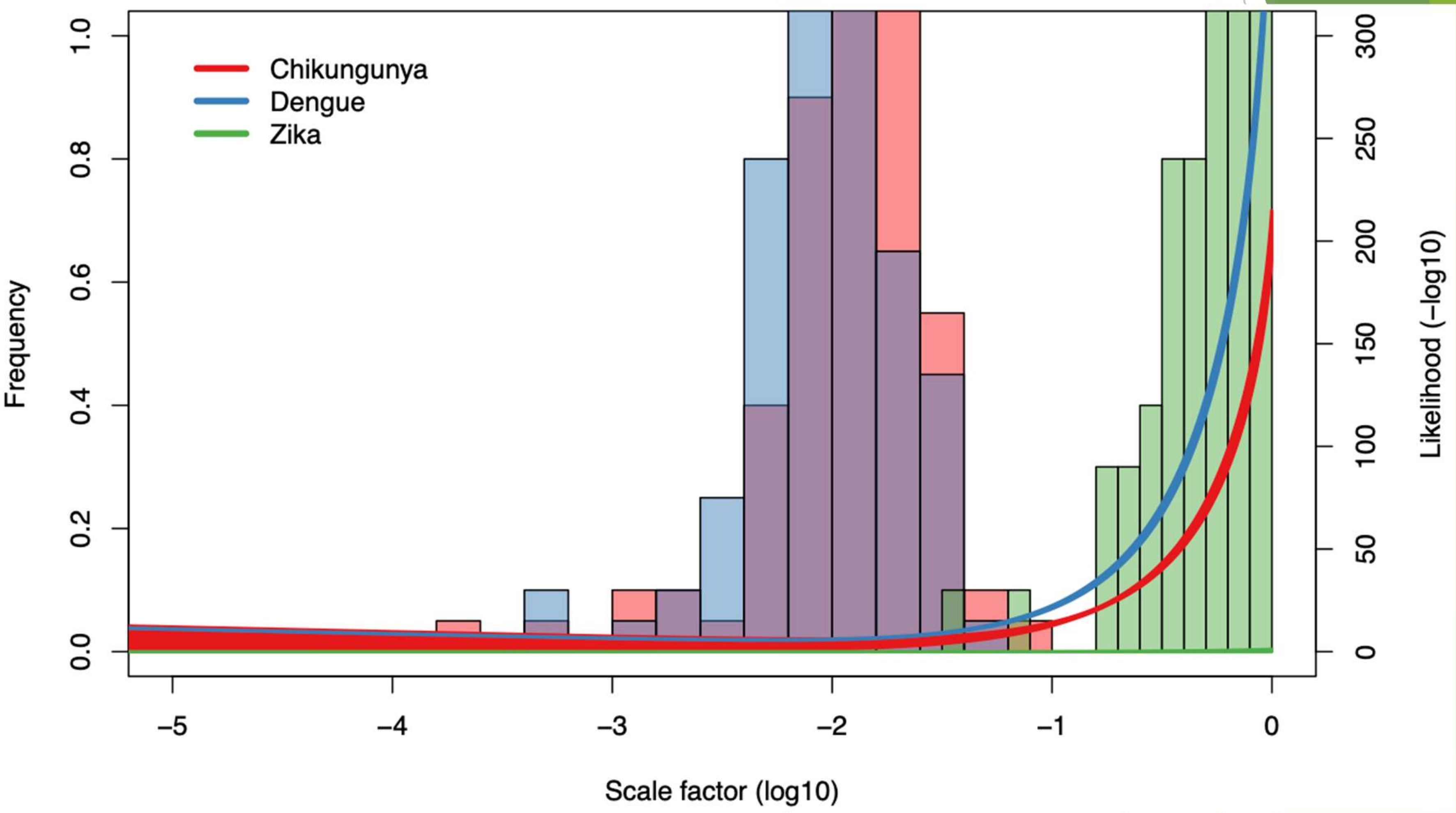
- 2020



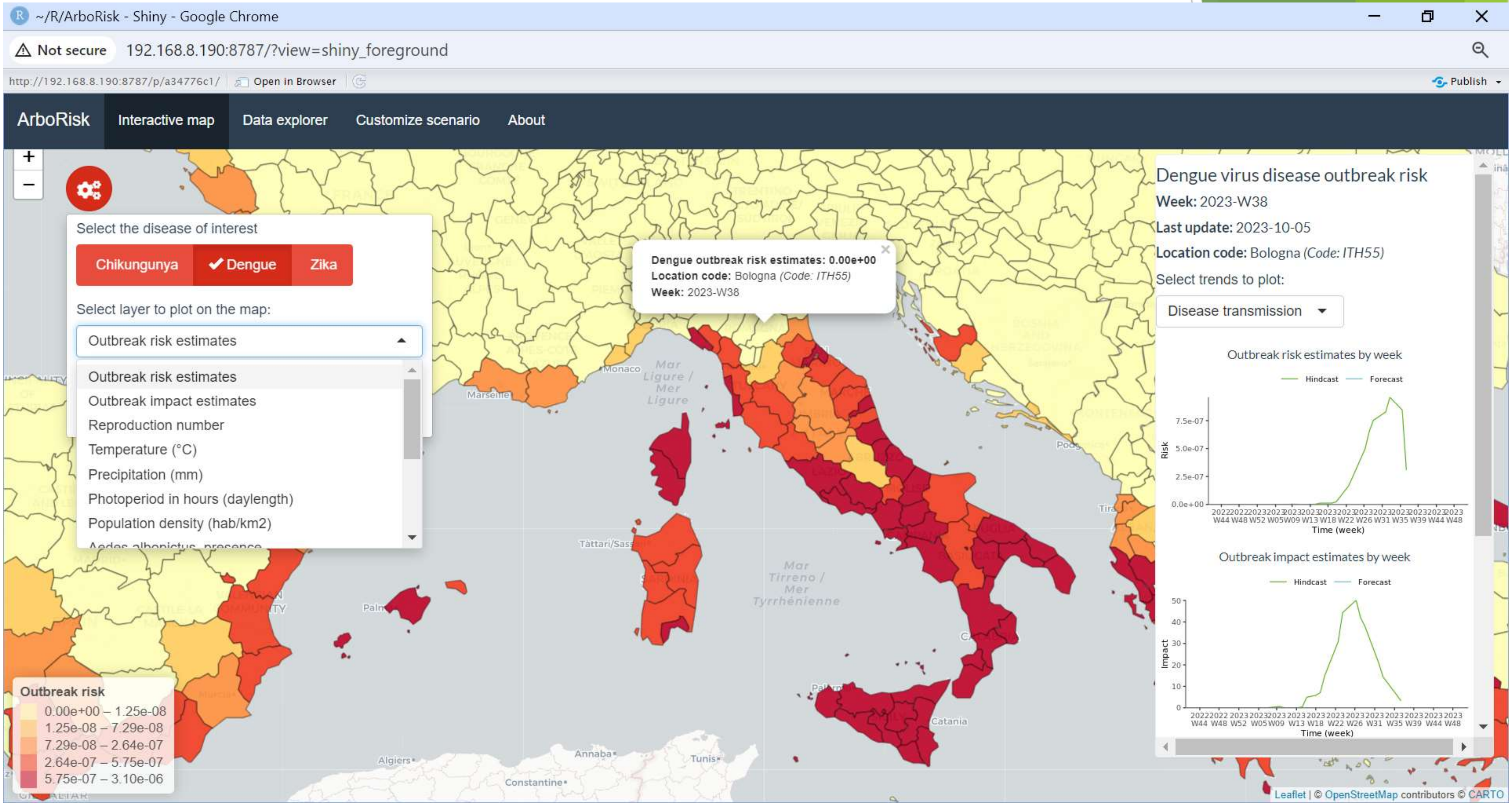
Probability of none to cause an outbreak

Probability of at least one to cause an outbreak

- 2020

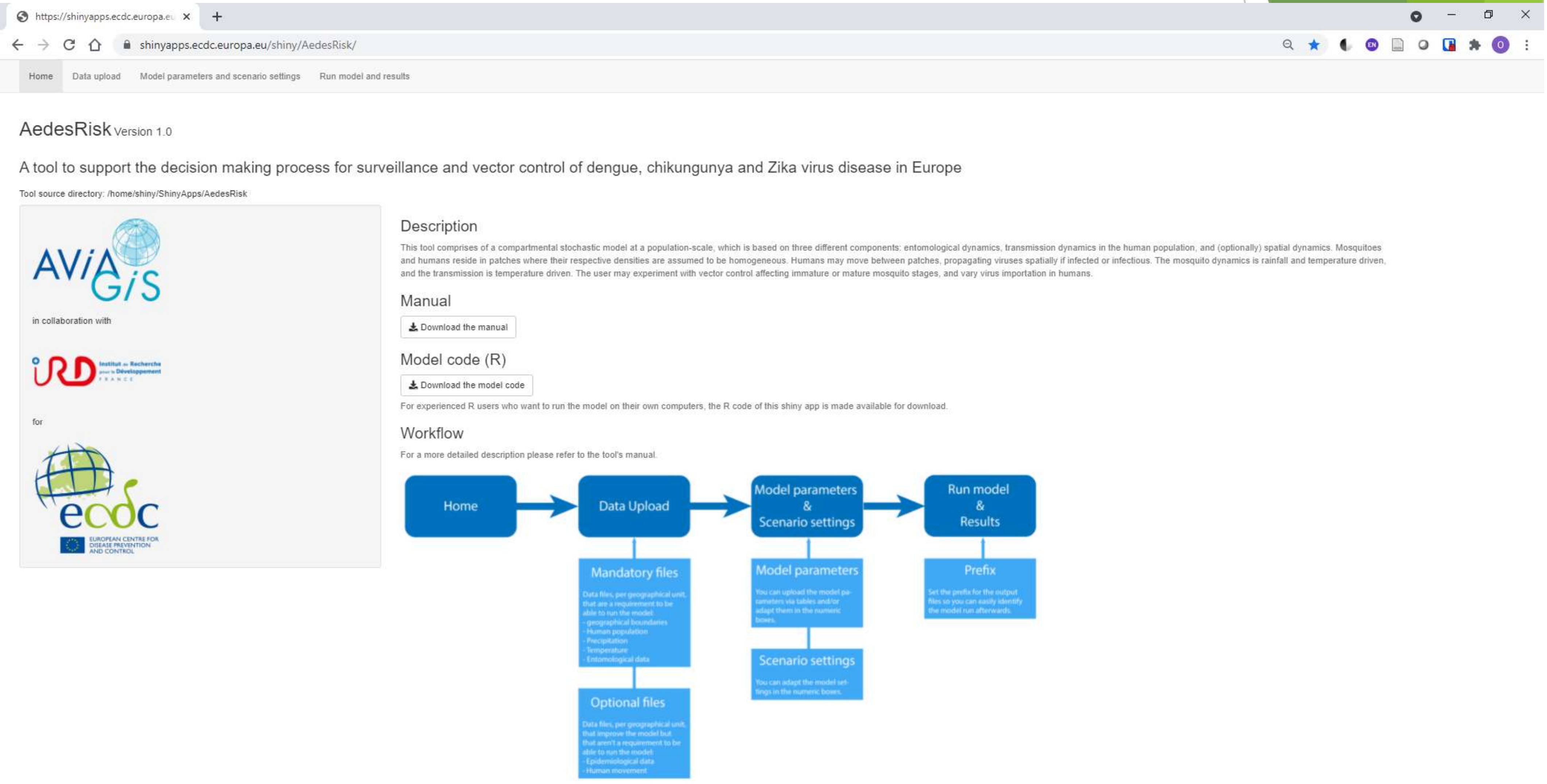


Chikungunya
Dengue
Zika
Frequency
0.0
0.2
0.4
0.6
0.8
1.0
Likelihood (−log10)
0
50
100
150
200
250
300
−5
−4
−3
−2
−1
0
Scale factor (log10)


~/R/ArboRisk - Shiny - Google Chrome
Not secure
192.168.8.190:8787/?view=shiny_foreground
http://192.168.8.190:8787/p/a34776c1/
Open in Browser
Publish
ArboRisk
Interactive map
Data explorer
Customize scenario
About
Select the disease of interest
Chikungunya
Dengue
Zika
Select layer to plot on the map:
Outbreak risk estimates
Outbreak risk estimates
Outbreak impact estimates
Reproduction number
Temperature (°C)
Precipitation (mm)
Photoperiod in hours (daylength)
Population density (hab/km2)
Dengue outbreak risk estimates: 0.00e+00
Location code: Bologna (Code: ITH55)
Week: 2023-W38
Dengue virus disease outbreak risk
Week: 2023-W38
Last update: 2023-10-05
Location code: Bologna (Code: ITH55)
Select trends to plot:
Disease transmission
Outbreak risk estimates by week
Hindcast
Forecast
Risk
Time (week)
Outbreak impact estimates by week
Impact
Outbreak risk
0.00e+00 – 1.25e-08
1.25e-08 – 7.29e-08
7.29e-08 – 2.64e-07
2.64e-07 – 5.75e-07
5.75e-07 – 3.10e-06
Leaflet | © OpenStreetMap contributors © CARTO

Scenario modelling at ECDC

https://shinyapps.ecdc.europa.eu/shiny/AedesRisk/

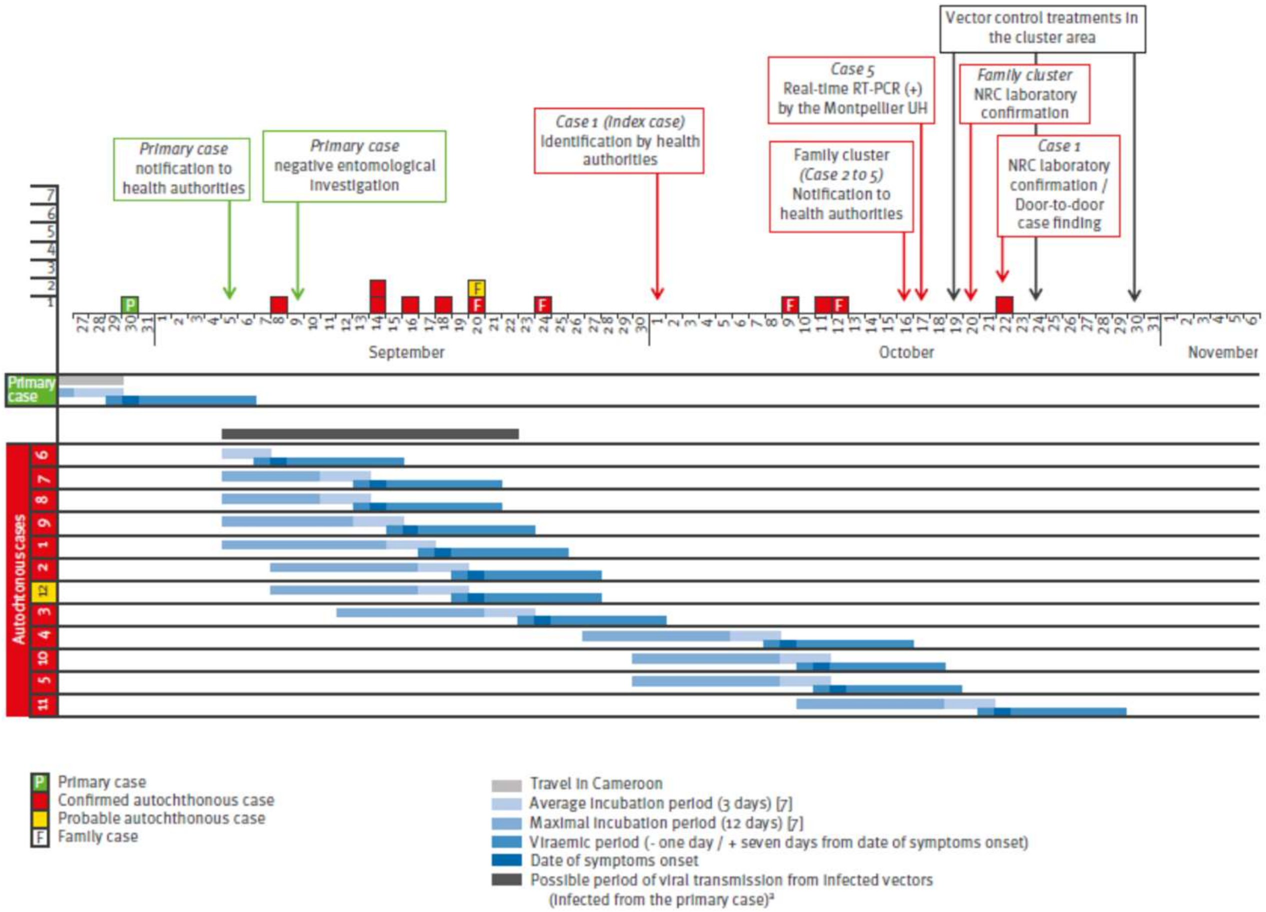


Chikungunya outbreak in Montpellier, France, September to October 2014

E Delisle (delisle.elsa@gmail.com)[1], C Rousseau[1], B Broche[2], I Leparc-Goffart[3], G L'Ambert[4], A Cochet[1], C Prat[3], V Foulongne[5], J B Ferré[4], O Catelinois[1], O Flusin[3], E Tchernonog[5], I E Moussion[2], A Wiegandt[2], A Septfons[6], A Mendy[2], M B Moyano[2], L Laporte[2], J Maurel[2], F Jourdain[7], J Reynes[5], M C Paty[7], F Golliot[1]

Figure

Timeline of symptoms onset for imported and autochthonous cases of chikungunya and epidemiological features, Montpellier, France, September–October 2014 (n = 13)

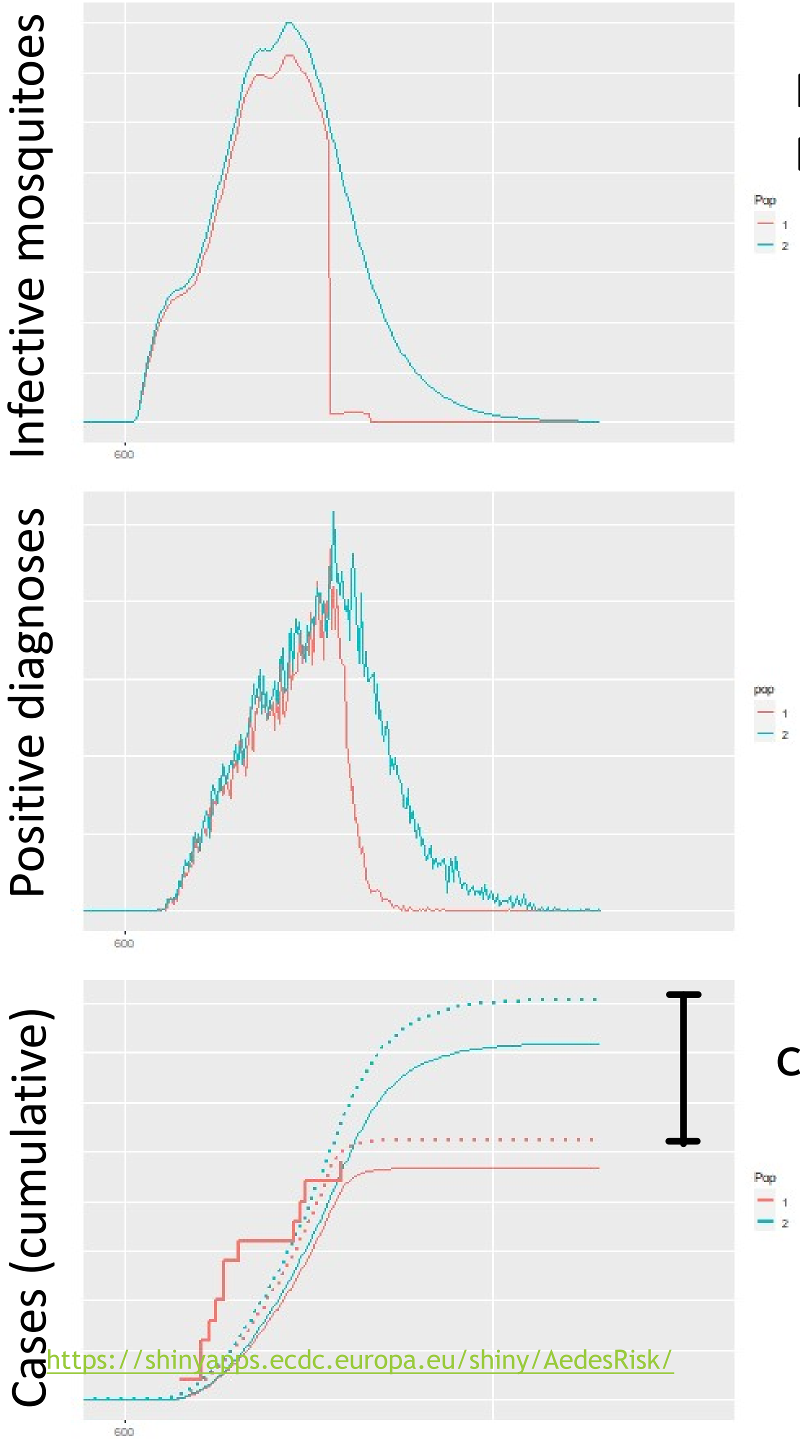


NRC: National Reference Center; RT-PCR: reverse transcriptase-PCR; UH: University Hospital.

Cases numbered by order of identification.

Source : French Institute for Public Health Surveillance (Institut de veille sanitaire), 2014.

[a] Possible period of viral transmission from infected vector (infected from the primary case):- mosquitoes biting the primary case between the first day and the last day of his viraemic period, extrinsic incubation period: seven days [8], mosquito lifespan: 10 days [9].



Red: intervention as done

Blue: non-intervention counterfactual

cases prevented

Thick red line: observed cases

Dotted lines: infections in humans

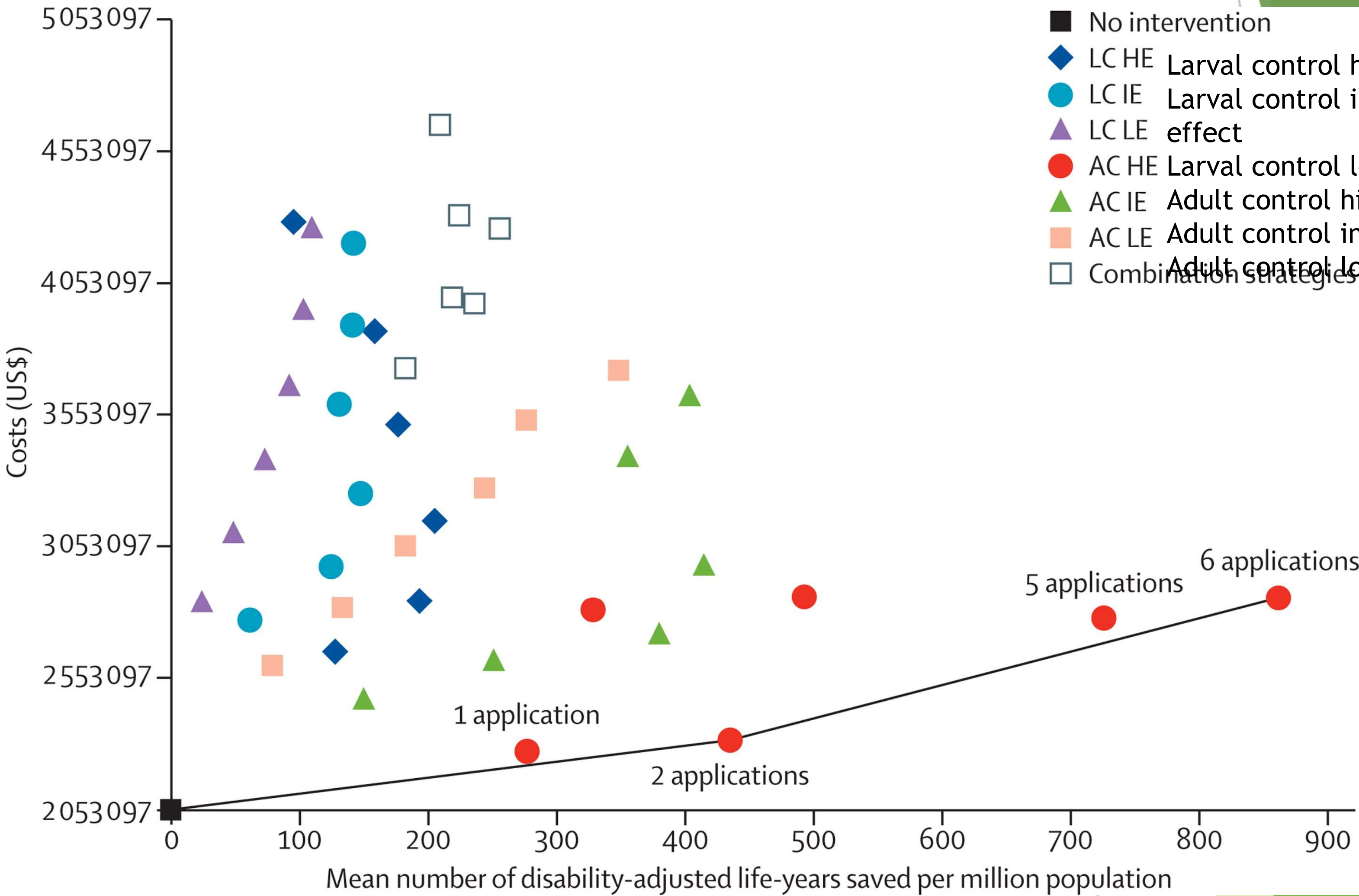
Solid lines: positive diagnoses

Cost-effectiveness

- What are the most effective and cost-effective (accepted) public-health strategies for mitigating the probability and impact of local transmission?

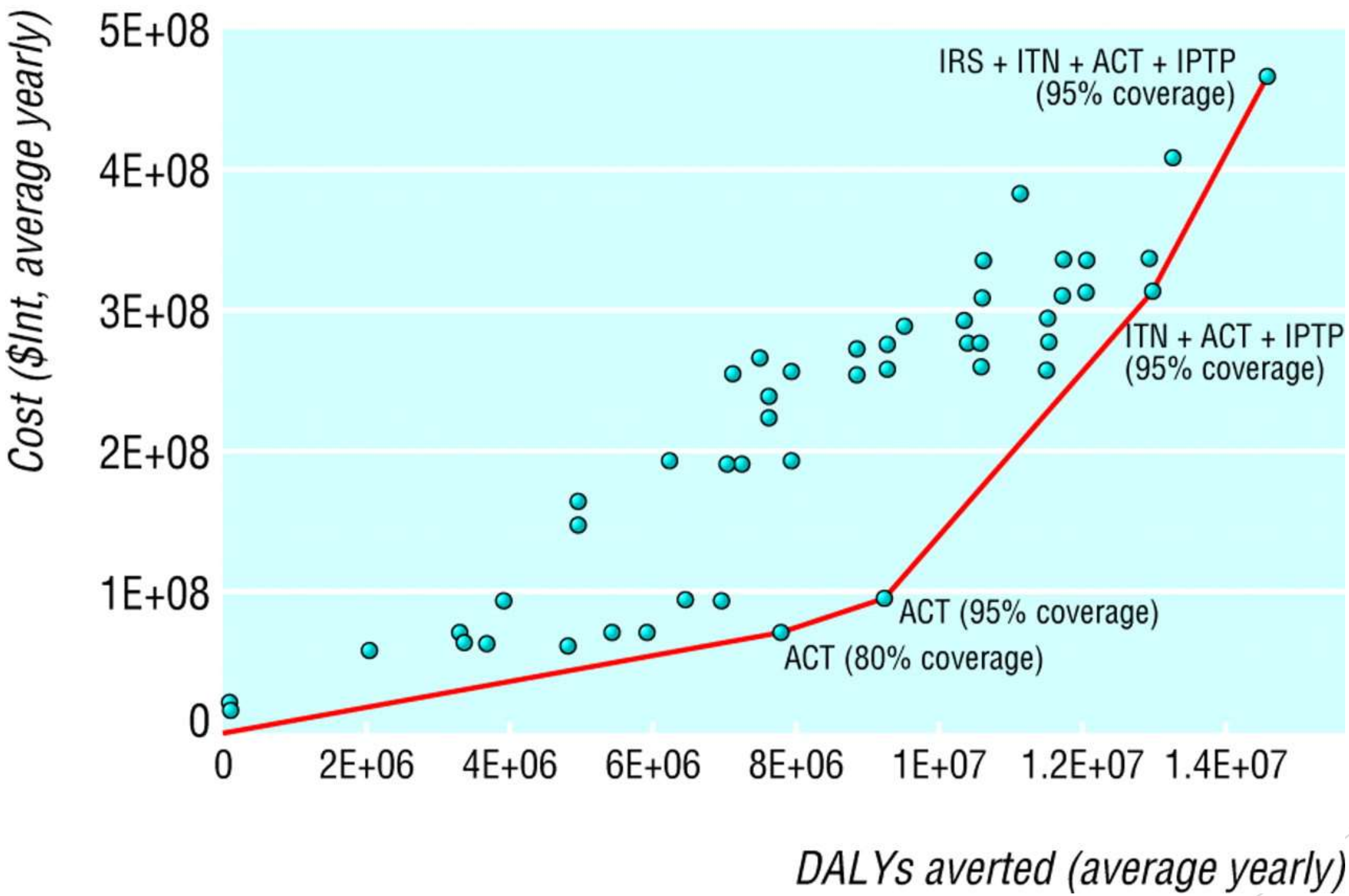
➢ Scenario-modelling combined with intervention cost-effectiveness data

Dengue vector control strategies in an urban setting: an economic modelling assessment



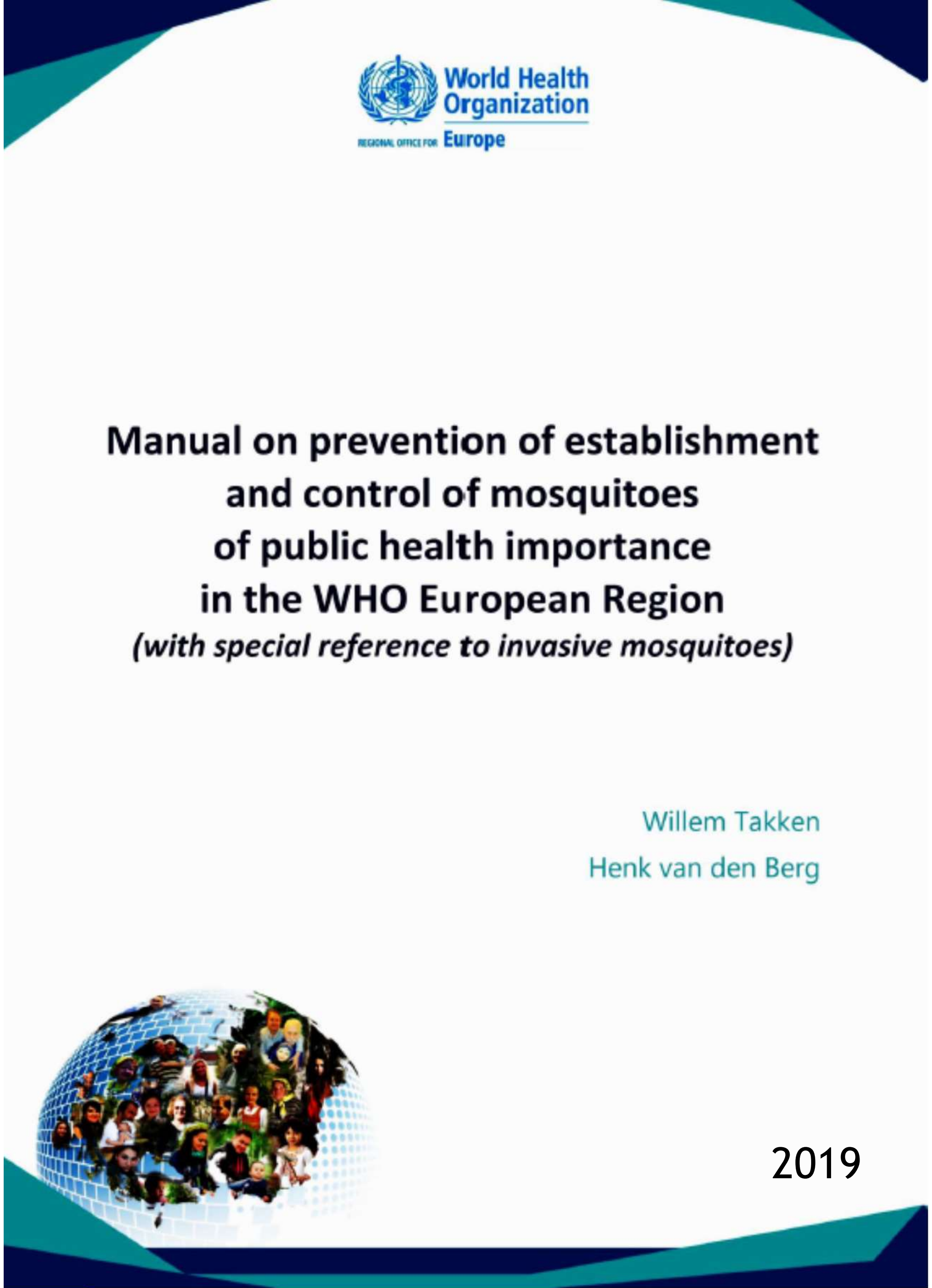
Mendes Luz et al., 2011
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60246-8/fulltext#

Cost-effectiveness plane showing 60 interventions against malaria analysed (20 interventions individually and combined at three assumed levels of coverage) and the expansion path, Afr-D



Morel et al. BMJ 2005;331:1299

ACT = Artemisinin combination therapy
IRS = Indoor residual spraying
ITN = Insecticide treated nets
IPTP = Intermittent preventive treatment during pregnancy



World Health Organization

REGIONAL OFFICE FOR Europe

Manual on prevention of establishment and control of mosquitoes of public health importance in the WHO European Region

(with special reference to invasive mosquitoes)

Willem Takken

Henk van den Berg

2019

"Recent systematic reviews of the **effectiveness** of vector control methods against *Ae. aegypti* and *Ae. albopictus* in the context of dengue control have concluded that there is a **paucity of reliable evidence**: there are few rigorous studies available on the impact of vector control on the vector population or on dengue incidence, and there is a need for standardized and comparative studies (Erlanger et al., 2008; Bowman et al., 2016).

As a result, we do not have a clear understanding of which of the currently available interventions actually work, nor of the conditions under which they work."

"Phase III studies should be designed around ***epidemiological endpoints*** to demonstrate the public health value of the intervention. ***Entomological outcomes cannot be used on their own for this purpose***, although they can be combined with epidemiological outcomes to evaluate a claimed entomological effect" (World Health Organization, 2017)

For Aedes-borne diseases in Europe, this is prohibitive: in order for epidemiological endpoints to provide significant results, this would require impossibly large and expensive studies, because of the low number of locally transmitted reported cases.

EXTERNAL SCIENTIFIC REPORT

VectorNet European Network for Medical and Veterinary Entomology

APPROVED: 23 June 2021

doi:10.2903/sp.efsa.2021.EN-6954

A systematic review to understand the value of entomological endpoints for assessing the efficacy of vector control interventions

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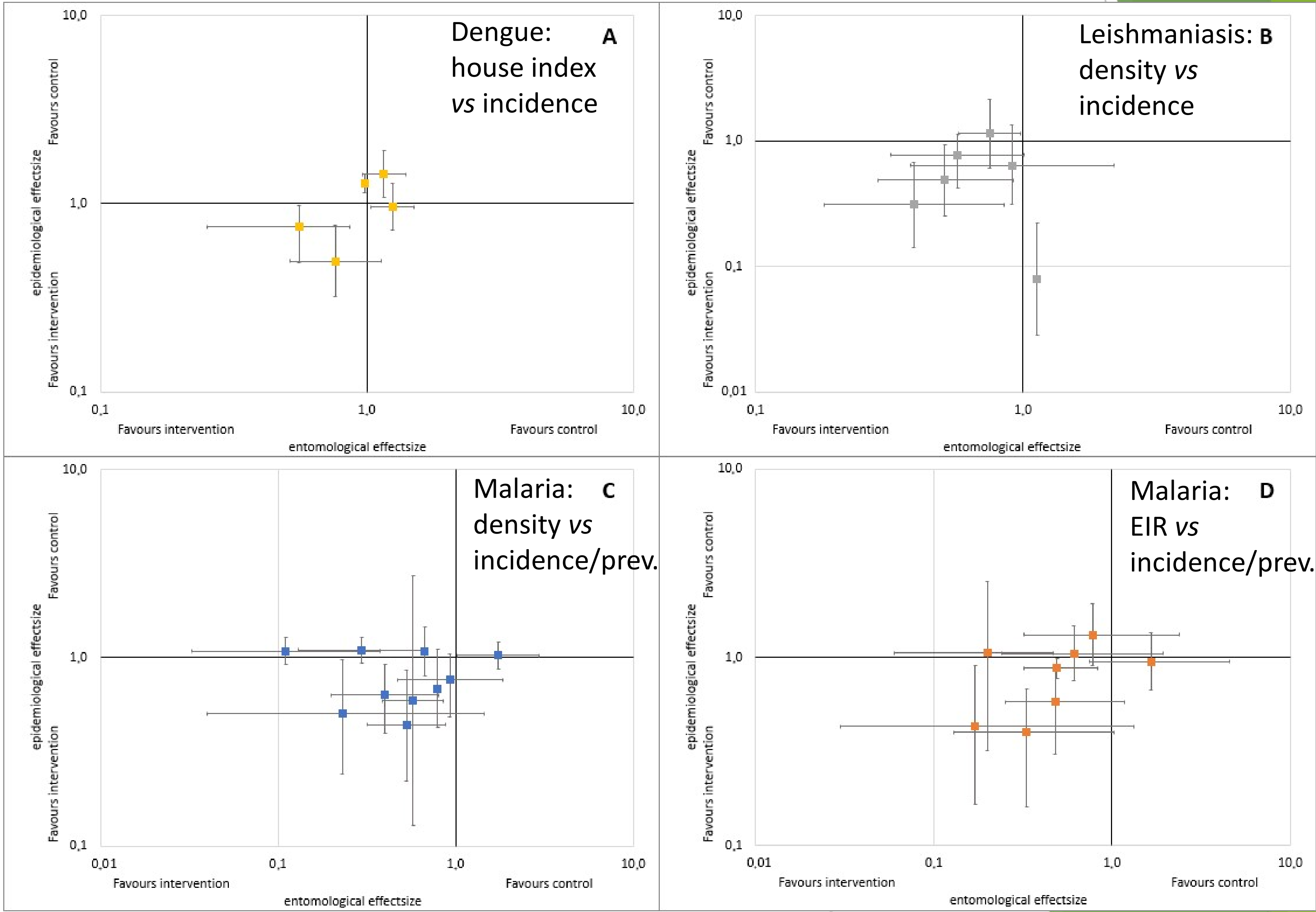
1. Institute of Tropical Medicine, Antwerp, Belgium
2. National Institute for Public Health and the Environment, Bilthoven, the Netherlands

Effectiveness: Entomological vs epidemiological endpoints



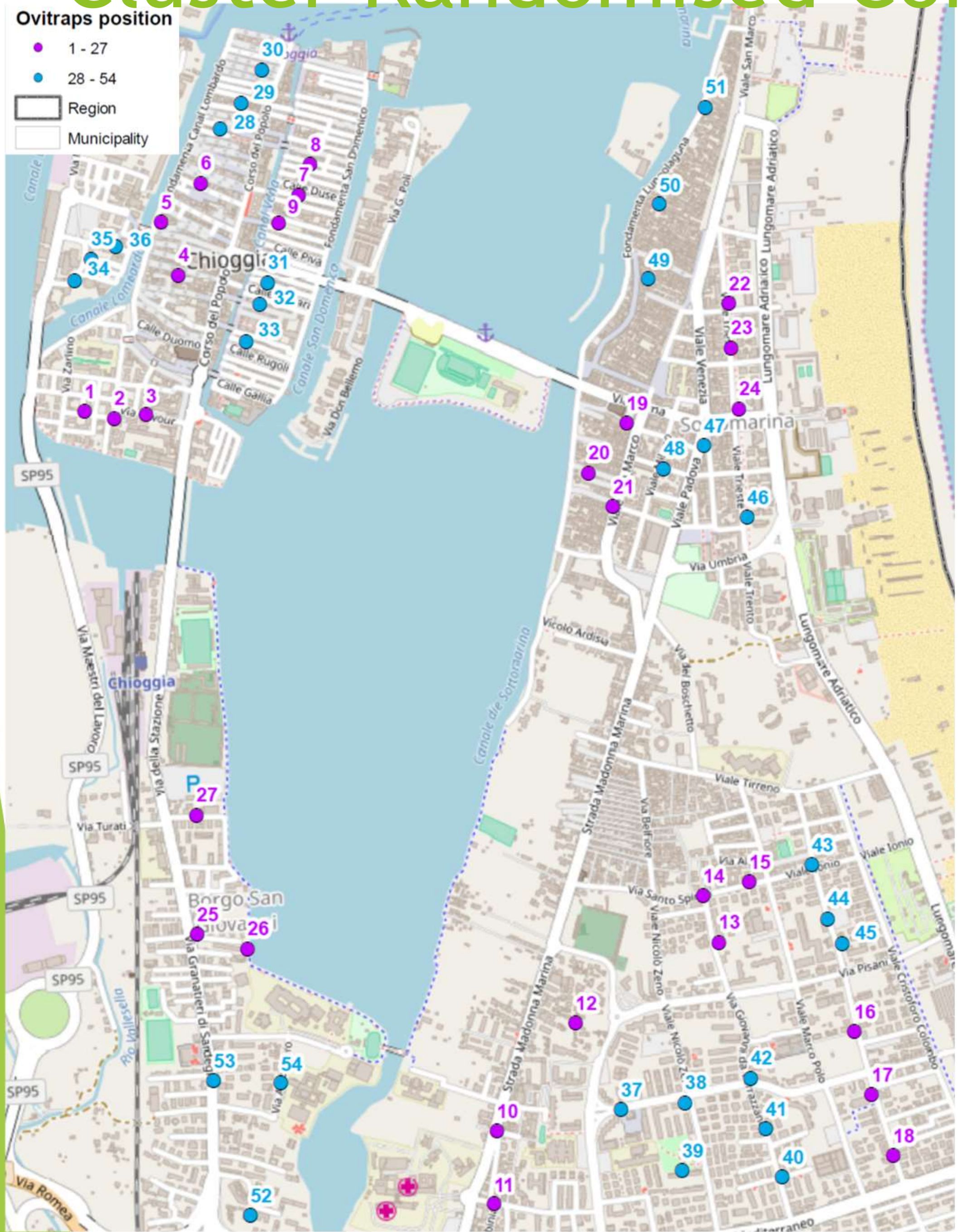
Cost-effectiveness analysis

- Is complex (and therefore error-prone), often requires modelling, and many assumptions.
- Needs to be specifically tailored to the setting and options under consideration
- Cost-effectiveness is not the only criterion for selection. Examples of other criteria:
  - Equity and other ethical considerations
  - Environmental considerations
  - Feasibility

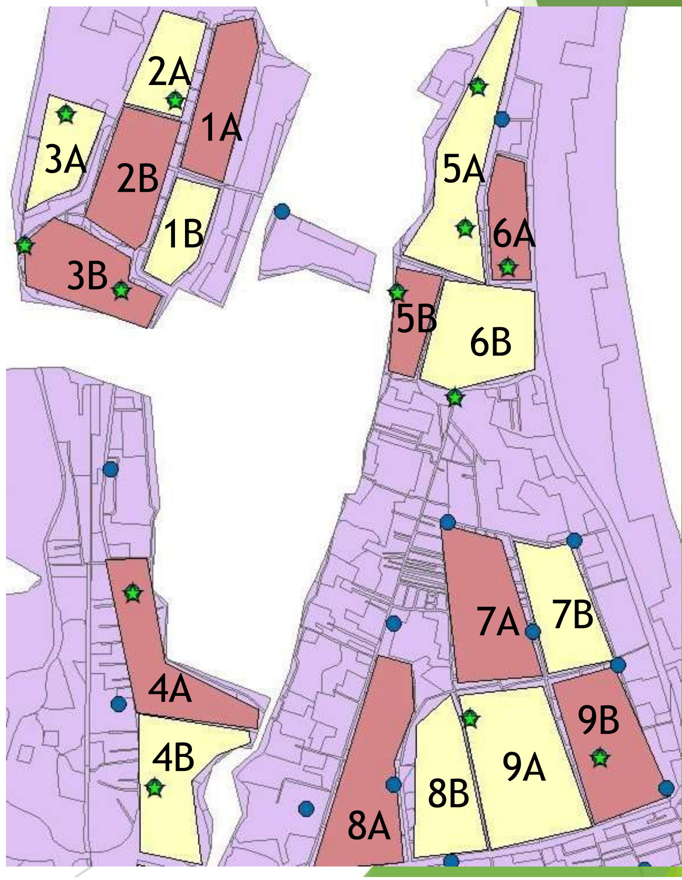
Effectiveness of larviciding (diflubenzuron) for *Ae. albopictus* in Chioggia, Italy

An environment where catch basins are an important breeding site for *Ae. albopictus*

Chioggia: Entomological Pair-wise Cluster Randomised Controlled Trial

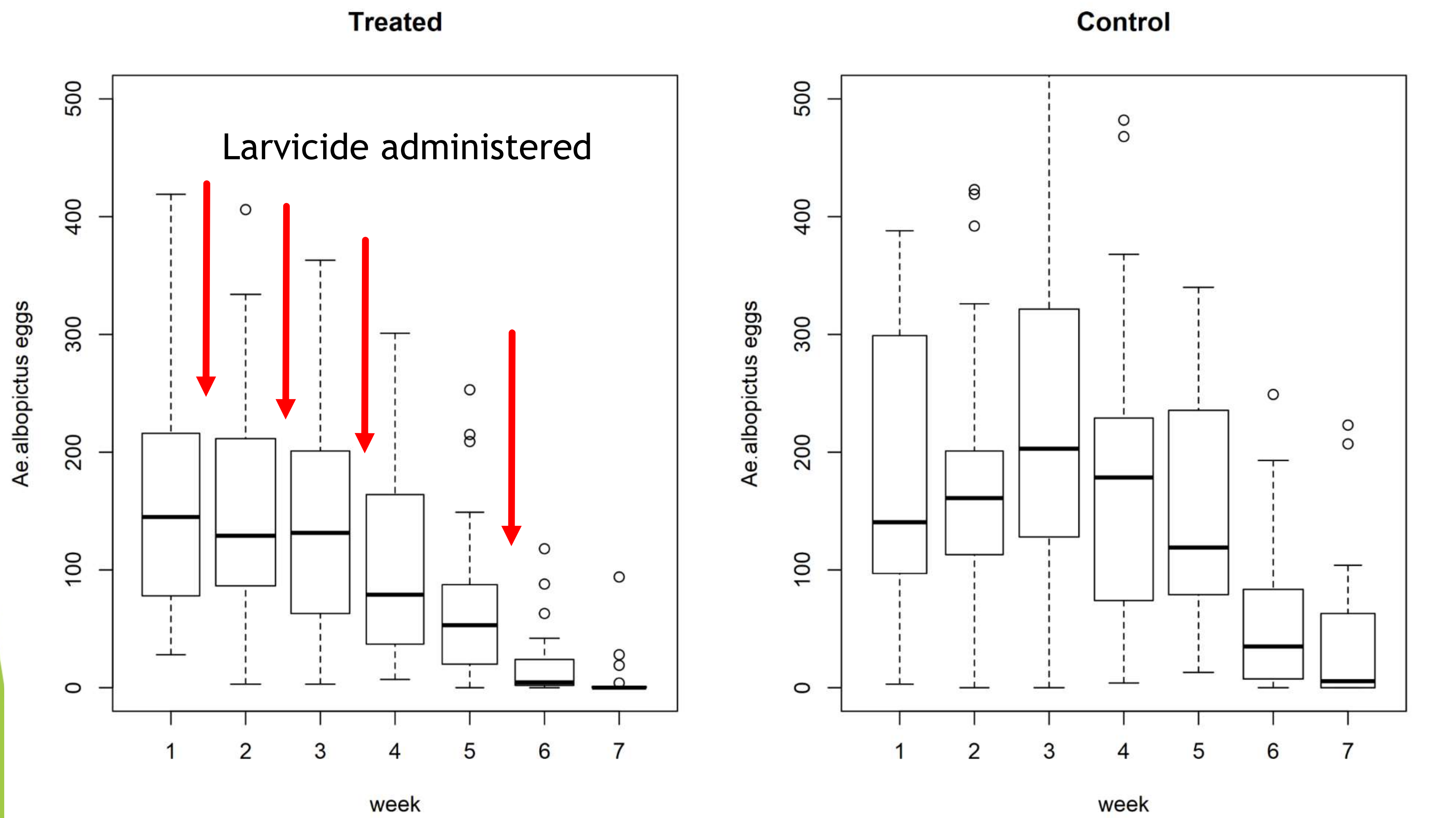


9 clusters: 9 treated areas, 9 untreated (control) areas
3 ovitraps in each
Duration: 6 weeks (07/08 to 16/10).
4 Treatments: 08/08, 28/08, 13/09, 15/10

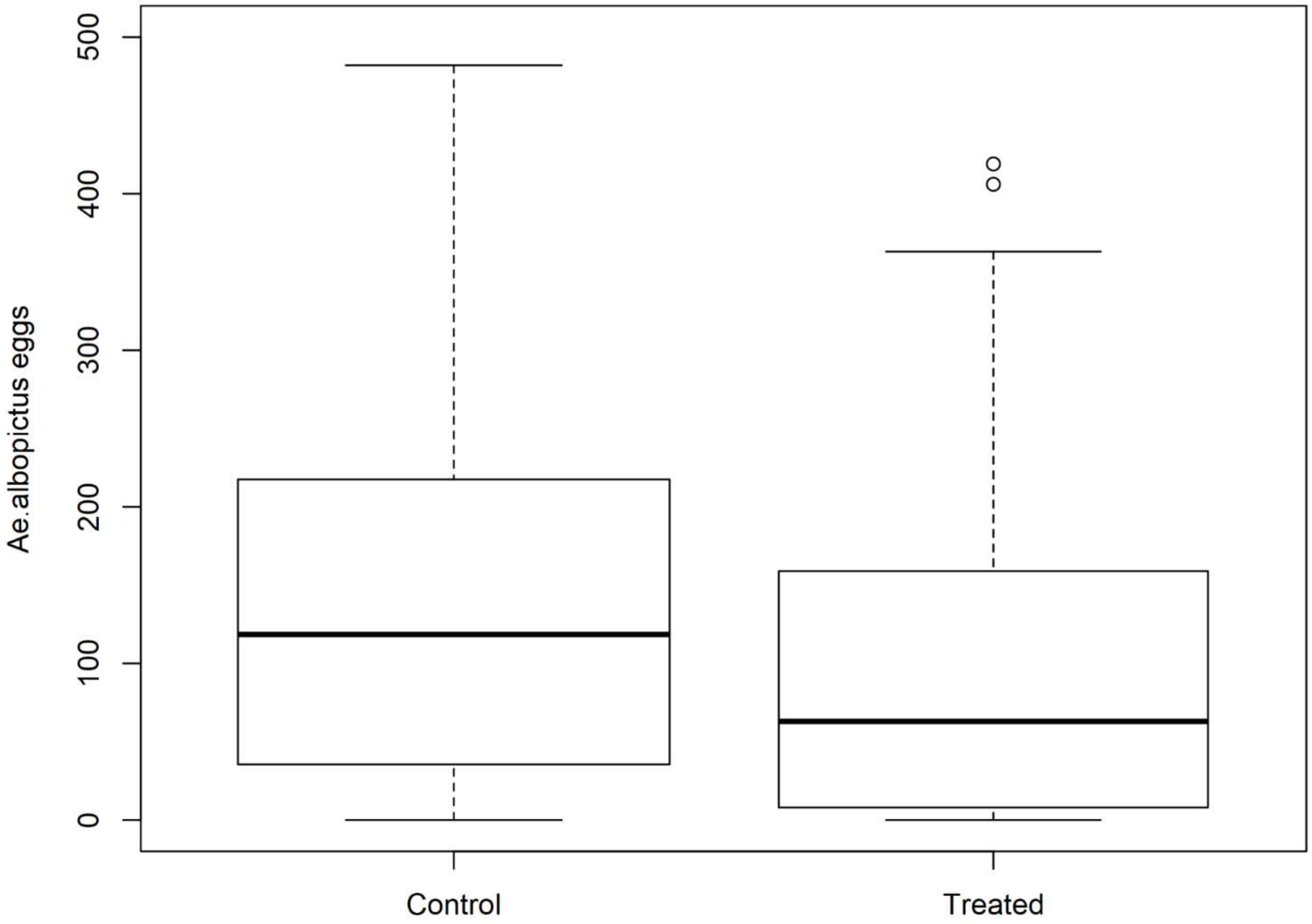


Light brown: treated / Yellow: untreated

Ovitrap temporal results



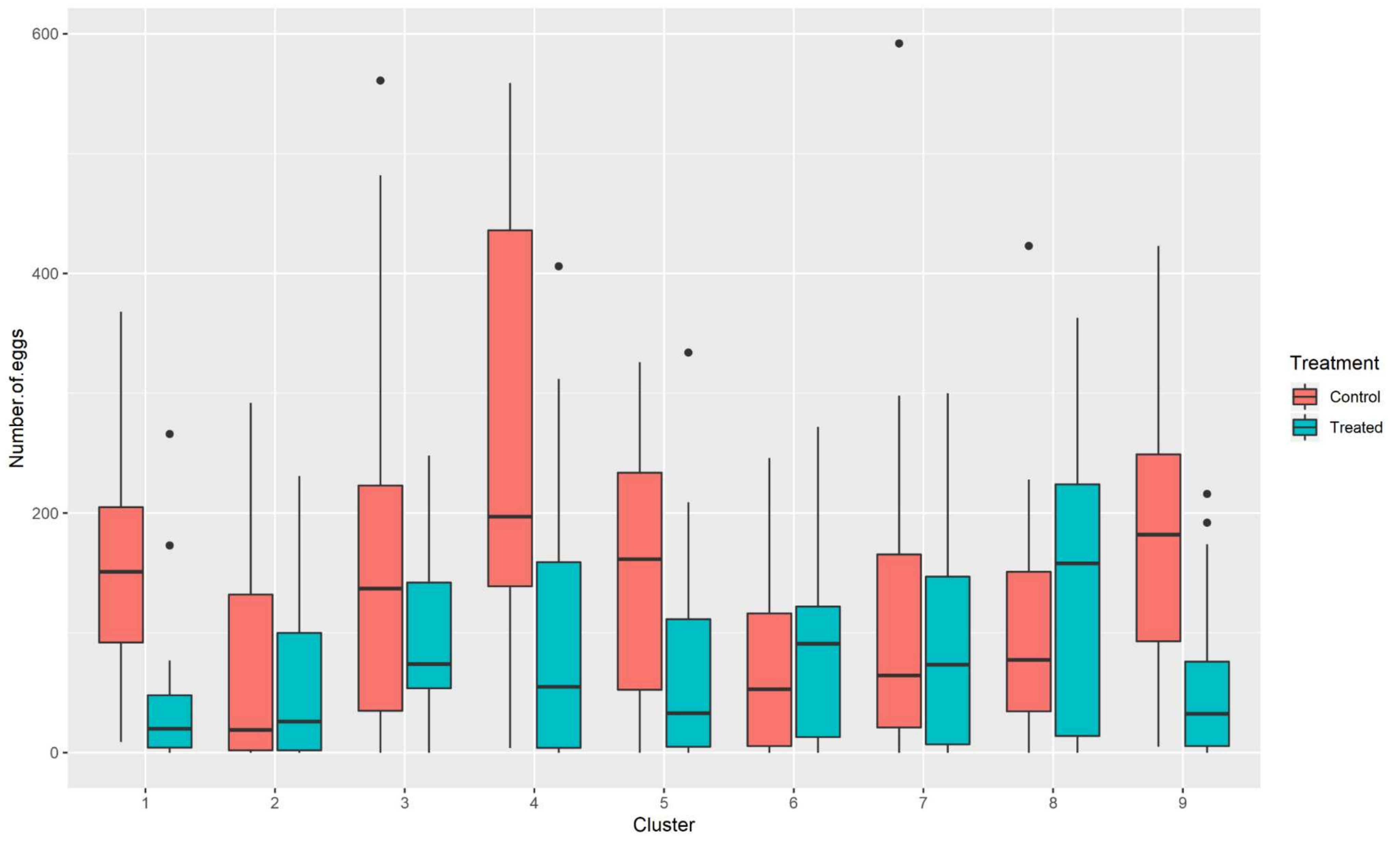
Ovitrap regression results



Negative binomial zero-inflated generalized linear mixed model with Cluster/Trap and Week as random effects

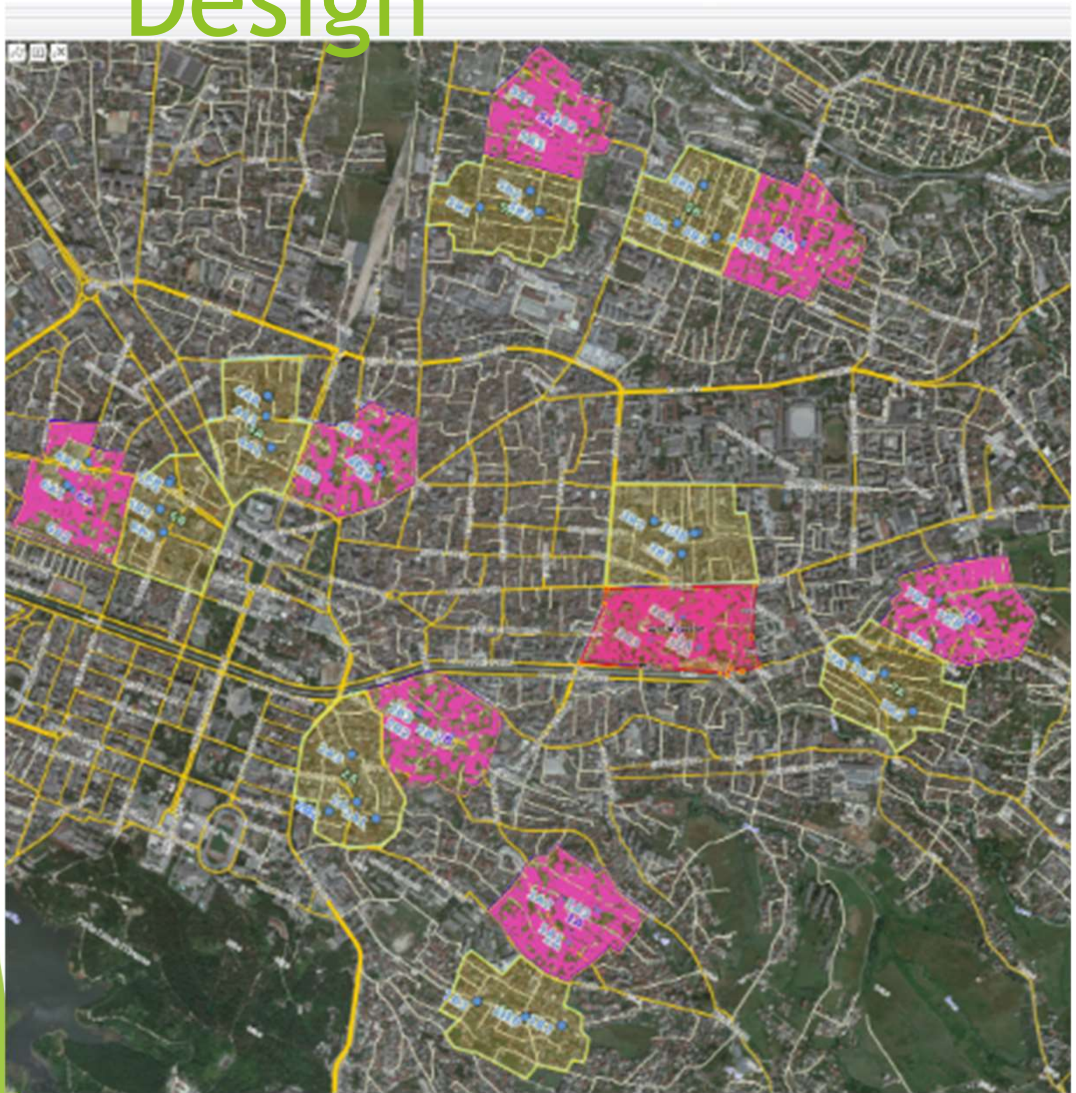
Incidence Rate Ratio = 0.46
p=0.00003

Differences in effect among cluster-pairs after first treatment: large variation



Entomological Pair-wise Cluster Randomised Controlled Trial in Tirana, Albania

Design

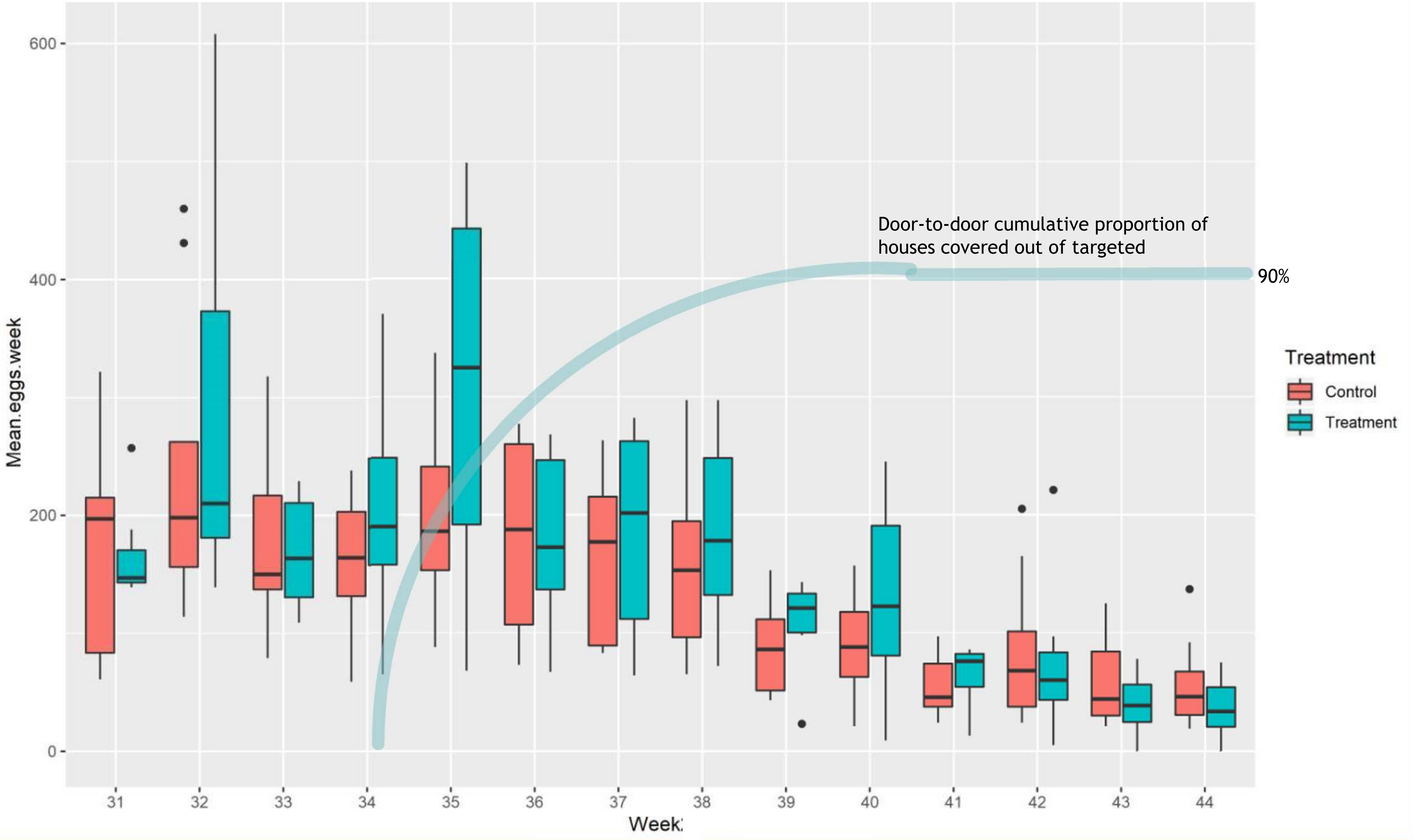


Eight cluster pairs
- 8 door-to-door/IVM areas
- 8 untreated (control) areas

Monitoring:
3 ovitraps and 1 BG-Sentinel trap in each cluster

Duration: 13 weeks monitoring

Ovitrap temporal results



Negative binomial Zero Inflated GLMM with random effects for Cluster/trap and Week

1 week lag: IRR=0.75, 95%CI 0.56–0.99

2 week lag: IRR=0.73, 95%CI 0.54–0.98

Lag between the interventions and the ovitrap sampling, related to the biological larval development time. IRR= incidence rate ratio

Conclusions

- Modelling plays an important role in risk assessment and planning of mitigation strategies
- There is insufficient evidence for **existing** entomological interventions
- Field studies with entomological outcomes specific to European setting could still be very useful as data input for models to aid strategic planning of vector control

Thank you for your attention and:

- Colleagues from ECDC, EFSA, VectorNet, ArboRisk and AedesRisk projects