Extra Lecture: Estimating the effective reproductive number at time {t}: R_t

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WHO R&D Blueprint to combat global pandemics

World Health Organization

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R&D Blueprint

The R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of research and development activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crises. With WHO as convener, the broad global coalition of experts who have contributed to the Blueprint come from medical, scientific and regulatory backgrounds. WHO Member States welcomed the development of the Blueprint at the World Health Assembly in May 2016.

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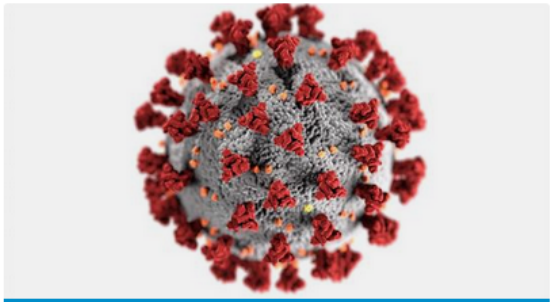
Key actions by disease



R&D Blueprint and COVID-19
R&D Blueprint and the Pandemic Response

- R&D Blueprint and Ebola/Marburg >
- R&D Blueprint and Lassa Fever >
- R&D Blueprint and MERS-CoV >
- R&D Blueprint and Nipah Virus >
- R&D Blueprint and Zika >

https://www.who.int/teams/blueprint/

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Volume 29, Number 7—July 2023

Dispatch

Estimates of Serial Interval and Reproduction Number of Sudan Virus, Uganda, August–November 2022

Valentina Marziano, Giorgio Guzzetta, Ira Longini, and Stefano Merler

Author affiliations: Bruno Kessler Foundation, Center for Health Emergencies, Trento, Italy (V. Marziano, G. Guzzetta, S. Merler); University of Florida, Colleges of Public Health and Health Professions and Medicine, Gainesville, Florida, USA (I. Longini)

Mathematical modeling of transmission to aid in vaccine trials assessment

Estimation of reproductive numbers:

- $Pois(\lambda)$ is a Poisson sample with rate λ;
- $C(t)$ is the projected daily number of new cases having symptom onset on t;
- $c(t)$ is the observed number of new cases having symptom onset on t;
- $\varphi(s)$ is the distribution of the generation time discretized by day, approximated with the estimated distribution of the serial interval;
- $\mathrm{R}(t)$ is the assumed reproduction number over time.

Master renewal equation

$$C(t) = \mathrm{Pois}\left(R(t)\sum_{s=1}^{t}\varphi(s)c(t-s)\right),$$

$$\mathrm{E}\{\mathrm{C(t)}|\ \mathrm{R(t)},\ \varphi(s), \mathbf{c(t-1)}\} = \mathrm{R(t)}\sum_{s=1}^{t}\varphi(s)\mathrm{c(t-s)}$$

Literature on estimating R_t

A Cori, NM Ferguson, C Fraser, S Cauchemez. A new framework and software to estimate time-varying reproduction numbers during epidemics. *Am J Epidemiol*, **178**(9):1505-1512, 2013

Wallinga J, Teunis P. Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Simi- lar Impacts of Control Measures. Am J Epidemiol. 2004; 160(6):509–16. https://doi.org/10.1093/aje/ kwh255 PMID: 15353409

Parag KV. Improved estimation of time-varying reproduction numbers at low case incidence and between epidemic waves. PLoS Comput Biol. 2021 Sep 7;17(9):e1009347. Doi: 10.1371/journal.pcbi.1009347. PMID: 34492011; PMCID: PMC8448340.

Chowell G, Hengartner NW, Castillo-Chavez C, Fenimore PW, Hyman JM. The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. J Theor Biol. 2004 Jul 7;229(1):119-26. doi: 10.1016/j.jtbi.2004.03.006. PMID: 15178190.

Wallinga J, Lipsitch M. How generation intervals shape the relationship between growth rates and reproductive numbers. Proc Biol Sci. 2007 Feb 22;274(1609):599-604. doi: 10.1098/rspb.2006.3754. PMID: 17476782; PMCID: PMC1766383.

Chowell G, Viboud C, Simonsen L, Moghadas SM. Characterizing the reproduction number of epidemics with early subexponential growth dynamics. J R Soc Interface. 2016 Oct;13(123):20160659. doi: 10.1098/rsif.2016.0659. PMID: 27707909; PMCID: PMC5095223.

Viboud C, Simonsen L, Chowell G. A generalized-growth model to characterize the early ascending phase of infectious disease outbreaks. Epidemics. 2016 Jun;15:27-37. doi: 10.1016/j.epidem.2016.01.002. Epub 2016 Feb 1. PMID: 27266847; PMCID: PMC4903879.

MINISTRY OF HEALTH

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Uganda

EBOLA VIRUS DISEASE

Republic of Uganda

Situation Report 93

Compiled on 11 January 2023 at 22 :00 HRS

Districts with confirmed cases

- Mubende
- Kassanda
- Kyegegwa
- Bunyangabu
- Kagadi
- Wakiso
- Masaka
- Kampala
- Jinja

Confirmed Cases

New: 00
Total: 142

Confirmed Deaths

New: 00
Cumulative: 55

Recoveries

New: 00
Cumulative: 87

Contacts

Active contacts: 00
Completed 21-days of follow-up: 4,793

Healthcare Worker Infections

New: 00
Cumulative: 19
Dead: 07

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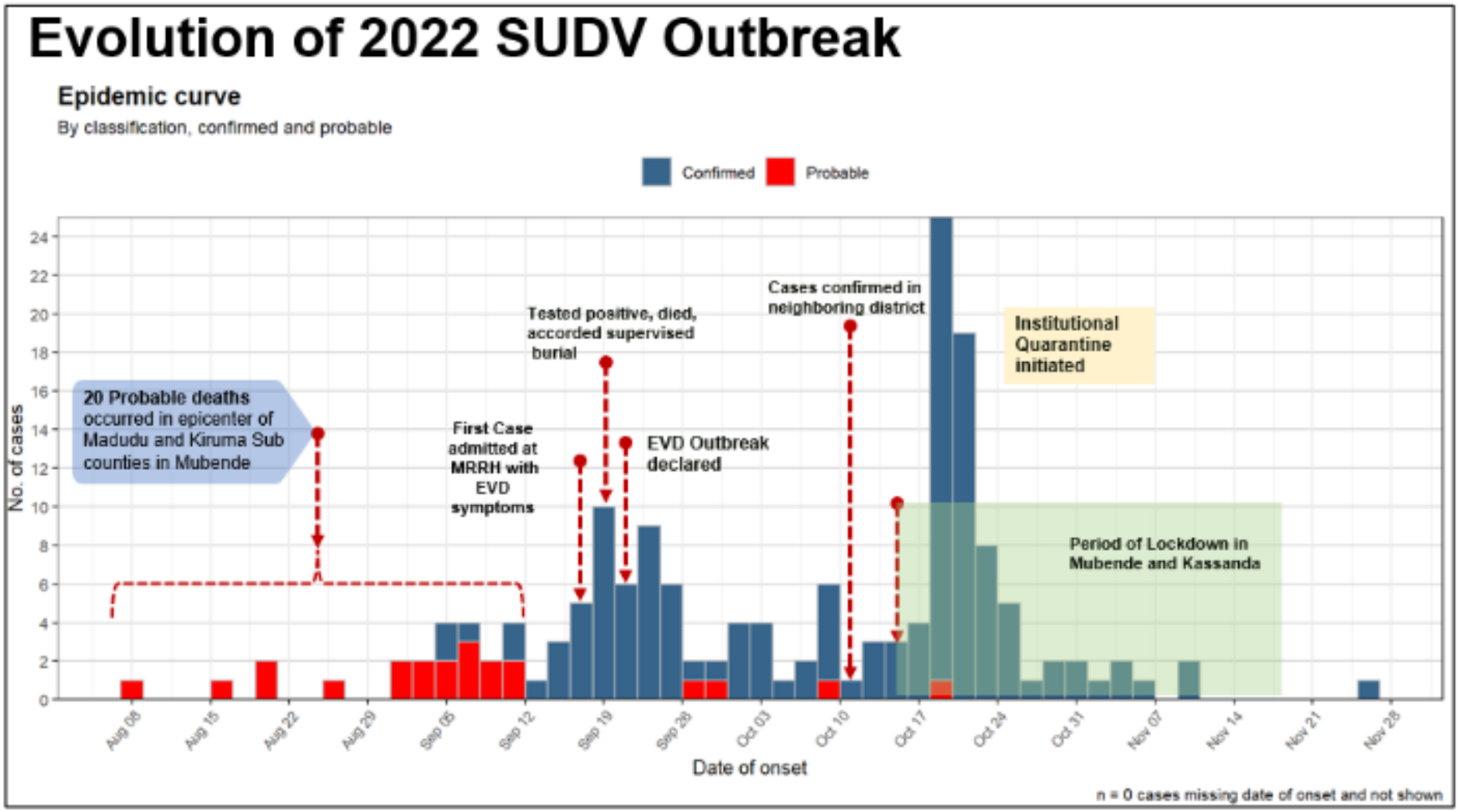
Powering research to prevent epidemics

Evolution of 2022 SUDV Outbreak



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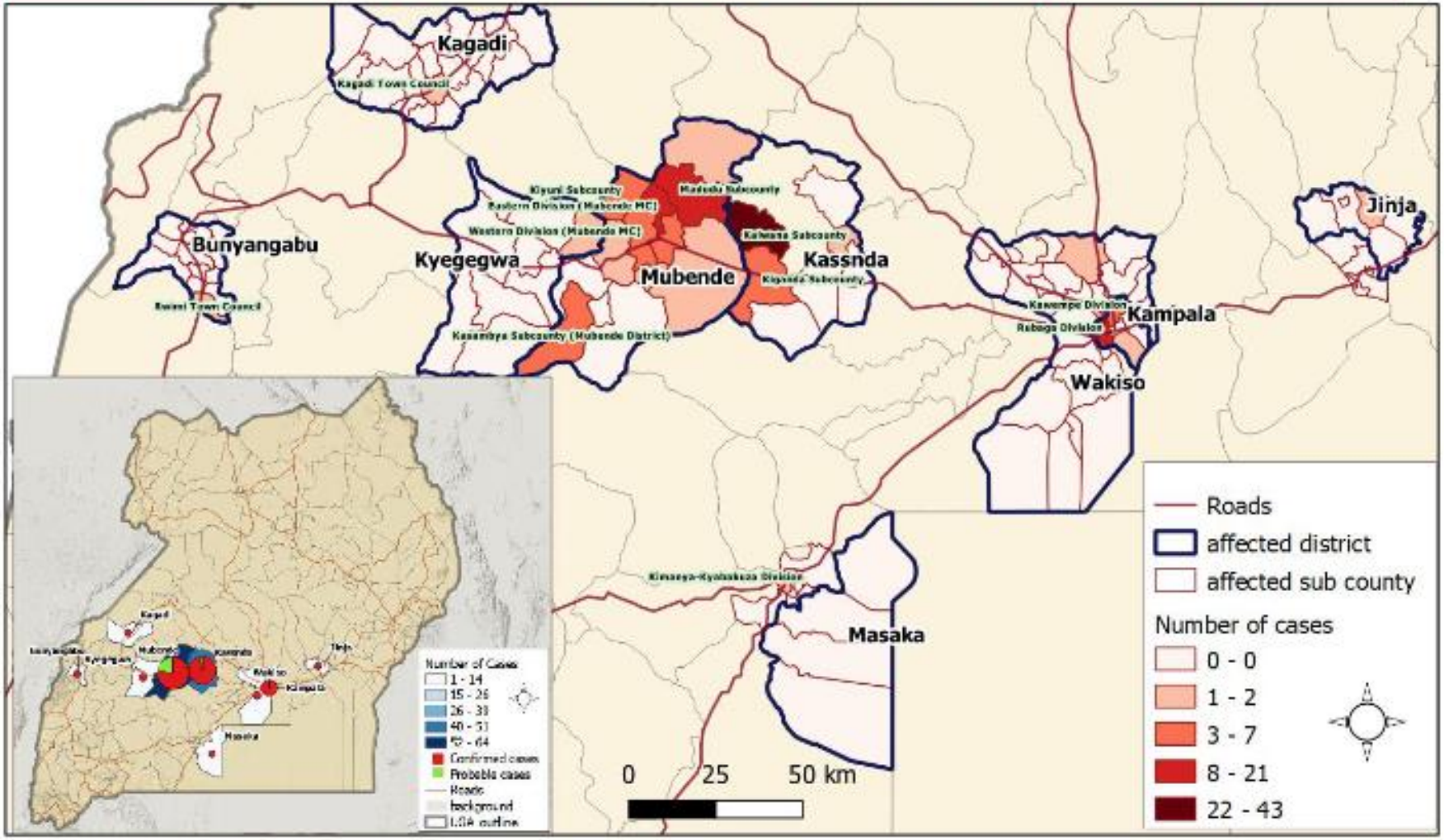
Place analysis of affected persons by district as of 11th January 2023



https://www.afro.who.int/sites/default/files/20231/Ug_EVD_SitRep%2393.pdf

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Preliminary estimates of Sudan virus transmissibility and projections of cases in Uganda, October 2022

October 17, 2022 - Valentina Marziano[1], Giorgio Guzzetta[1], Ira Longini[2],

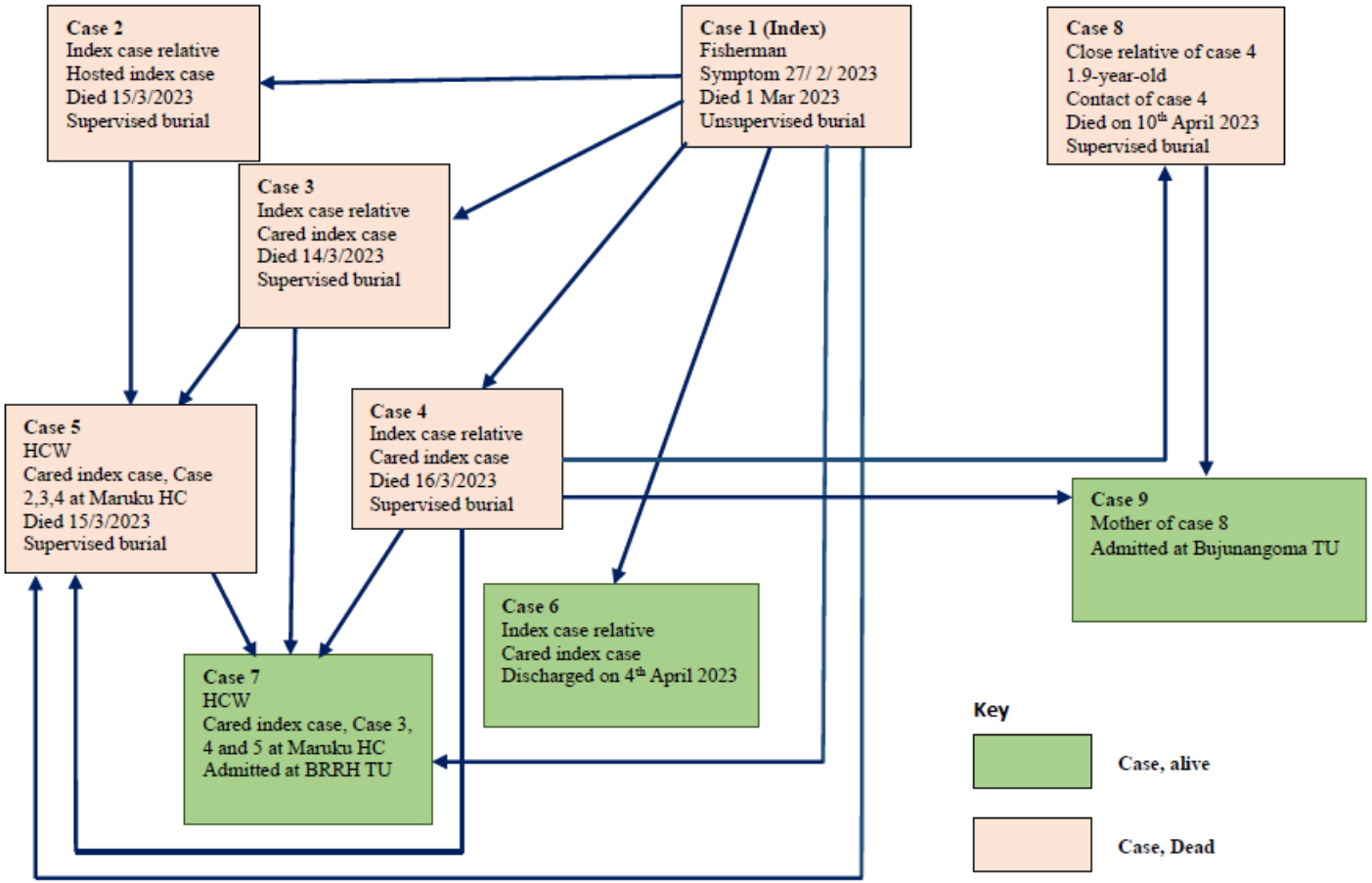
Stefano Merler[1] [1]Bruno Kessler Foundation, Trento, Italy; [2]University of

Florida, Gainesville, US

Summary

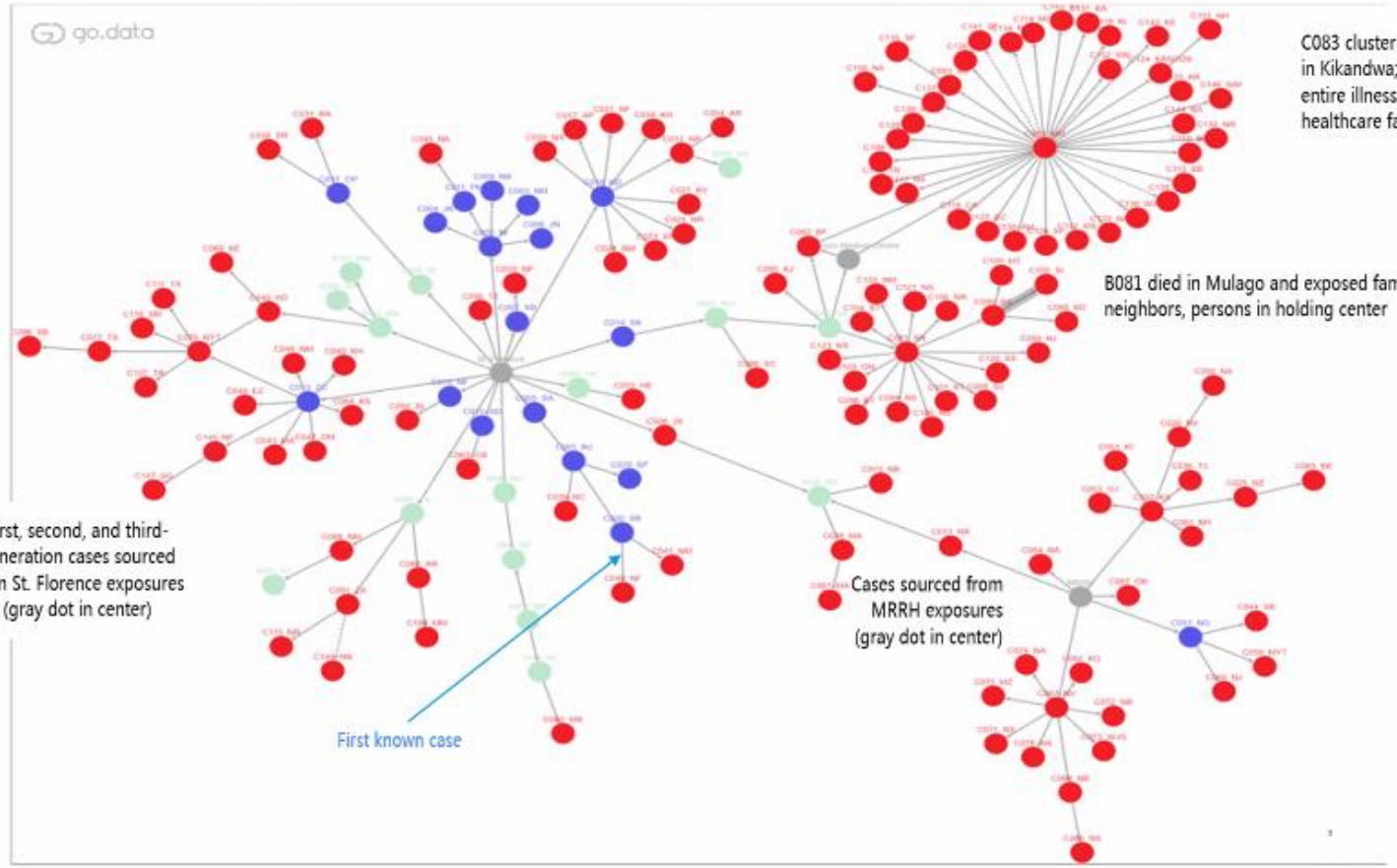
- We estimated the serial interval and reproduction numbers for the outbreak of Sudan virus currently spreading in Uganda.
  - The serial interval of the Sudan virus, estimated from data on the 2000-2001 outbreak in Uganda, is estimated to be Weibull distributed with mean 12 days (95% percentiles of the distribution: 4-24 days).
  - The basic reproduction number of the 2022 outbreak is estimated to be 3.7 on average, with broad confidence intervals (95% CI: 2.7-4.8).
  - After a peak reached around September 20, the net reproduction number R_t has declined below the epidemic threshold since the early days of October. This might depend on incompleteness of data, population awareness, interventions, or a combination of these factors.

Example


Case 2
Index case relative
Hosted index case
Died 15/3/2023
Supervised burial
Case 1 (Index)
Fisherman
Symptom 27/ 2/ 2023
Died 1 Mar 2023
Unsupervised burial
Case 8
Close relative of case 4
1.9-year-old
Contact of case 4
Died on 10th April 2023
Supervised burial
Case 3
Index case relative
Cared index case
Died 14/3/2023
Supervised burial
Case 5
HCW
Cared index case, Case 2,3,4 at Maruku HC
Died 15/3/2023
Supervised burial
Case 4
Index case relative
Cared index case
Died 16/3/2023
Supervised burial
Case 9
Mother of case 8
Admitted at Bujunangoma TU
Case 6
Index case relative
Cared index case
Discharged on 4th April 2023
Case 7
HCW
Cared index case, Case 3, 4 and 5 at Maruku HC
Admitted at BRRH TU
Key
Case, alive
Case, Dead

Estimation of serial

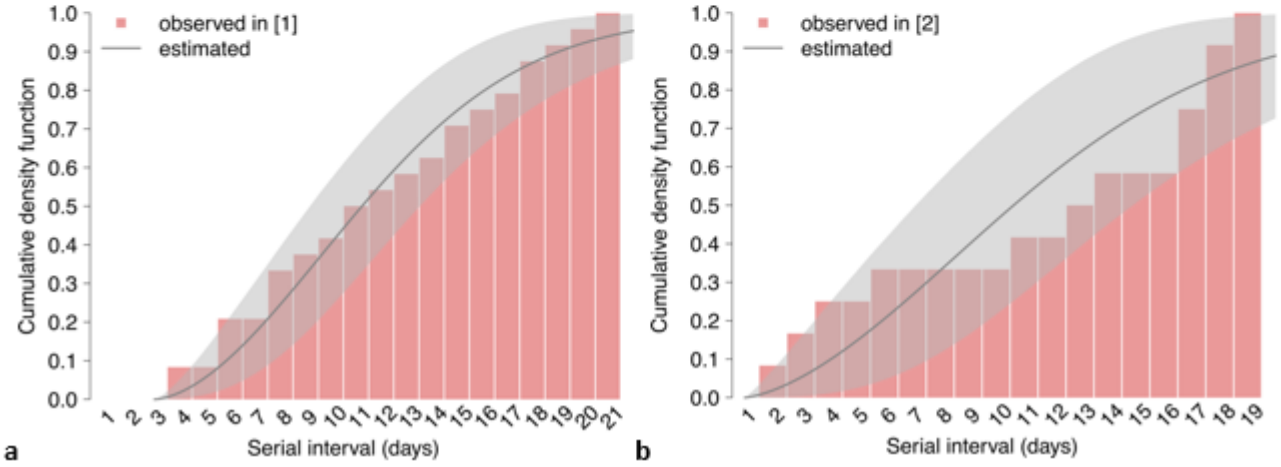
Transmission trees (as of 1 November 2022)



Estimation of serial interval

Table S2. Parameters of the Weibull distribution of the serial interval as estimated from the different datasets.

Dataset	2000-2001 SUDV outbreak [1] (n=24)	2022 SUDV outbreak [2] (n=12)
Offset (days)	3	1
Shape (mean)	1.76 (1.35-2.60)	1.63 (1.15-3.04)
Scale (95%CI)	10.14 (7.77-12.58)	11.97 (7.9-16.56)
Mean (95%CI) (days)	12 (10-14.2)	11.7 (8.2-15.8)
95%CI of the mean distribution (days)	4-24	2-28



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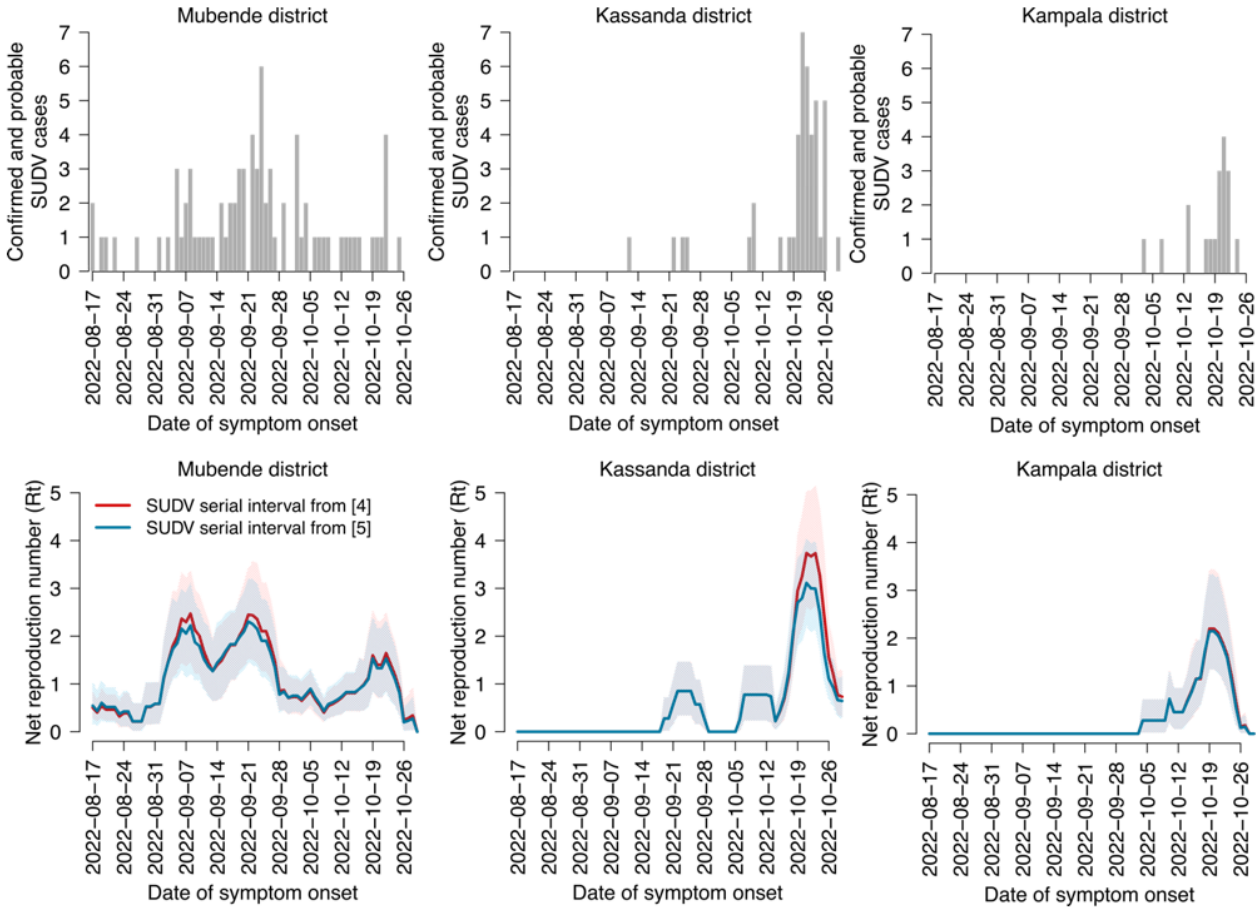
Estimates of R_t



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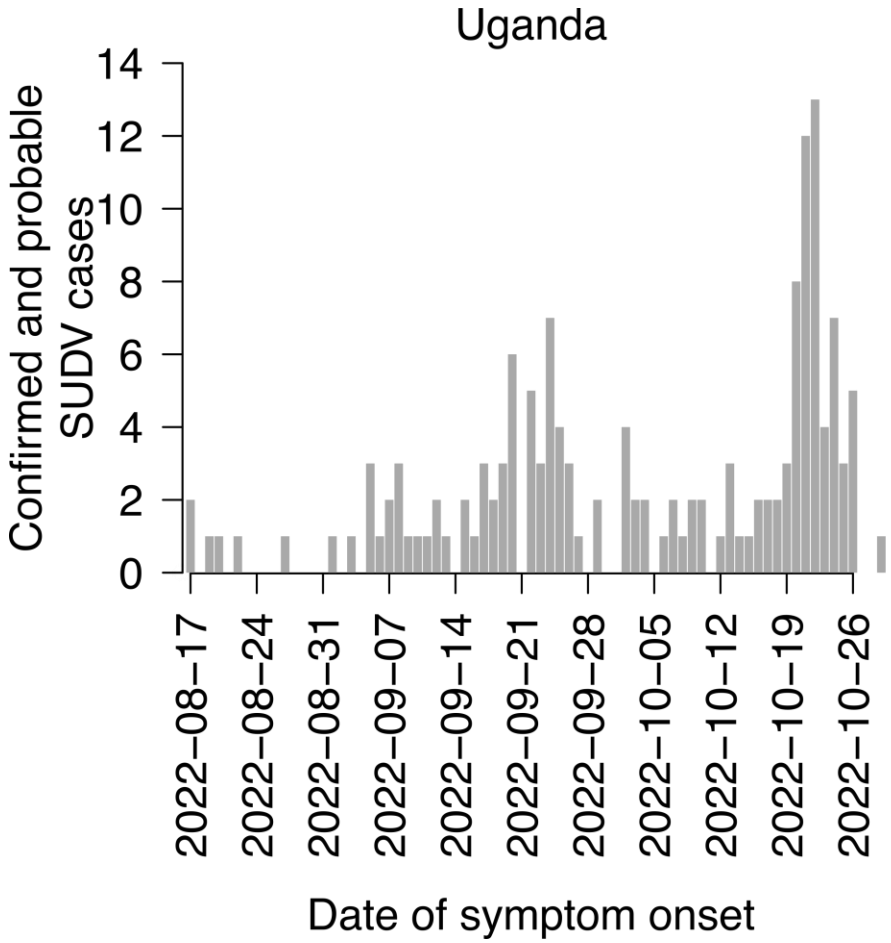

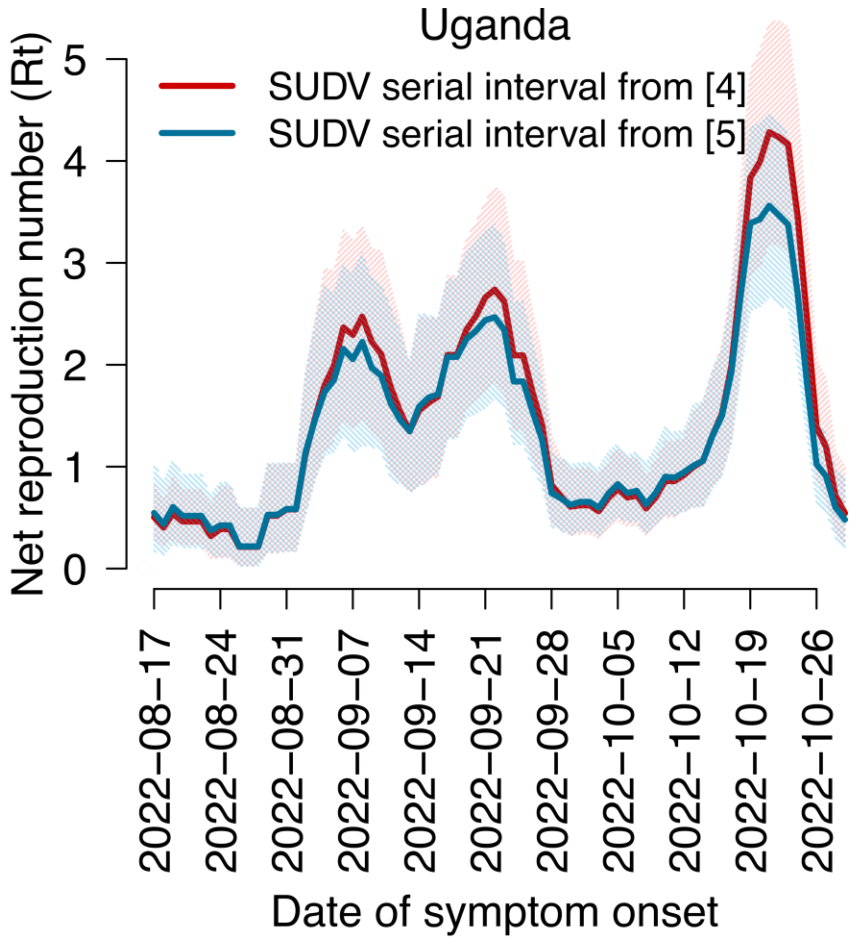

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Real time projections

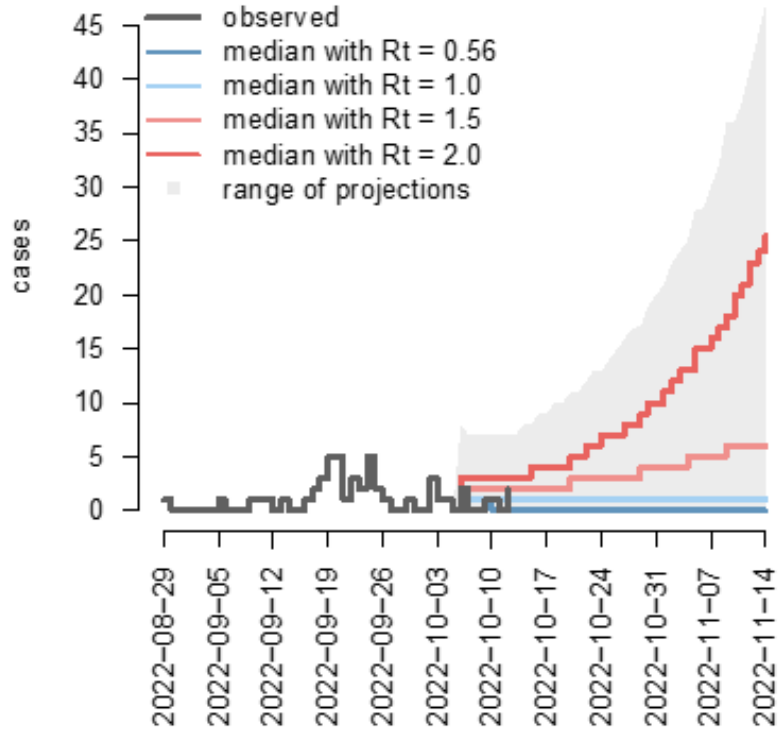

Figure 4. Projections of Sudan virus cases in Uganda by date of symptom onset under different scenarios for the mean reproduction number, assumed constant between October 5 and November 15.

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Thank You!