WHO Blueprint priority pathogen systematic reviews

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On behalf of the Imperial College Priority Pathogen group

MRC Centre for Global Infectious Disease Analysis

WHO Collaborating Centre for Infectious Disease modelling

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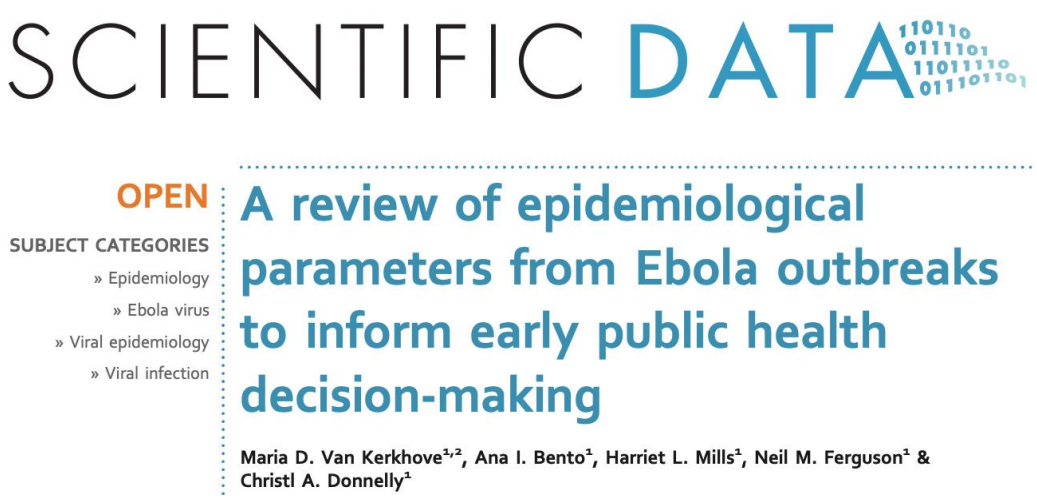
Rationale and overview

- MRC Centre for Global Infectious Disease Analysis
- WHO collaborating centre for modelling, aiming to provide rapid analysis of urgent infectious disease threats

- Typically designing ID models from early on in epidemics to answer important public health questions

→ Requires rapidly compiling current knowledge on a given pathogen


SCIENTIFIC DATA

OPEN

SUBJECT CATEGORIES
» Epidemiology
» Ebola virus
» Viral epidemiology
» Viral infection

A review of epidemiological parameters from Ebola outbreaks to inform early public health decision-making

Maria D. Van Kerkhove[1,2], Ana I. Bento[1], Harriet L. Mills[1], Neil M. Ferguson[1] & Christl A. Donnelly[1]

→ We often do this in real-time, but we could
  → Be proactive
  → Generate a "live" database of parameter values
  → For "important" pathogens

→ Project started in 2019, using the WHO blueprint priority disease list at the time

→ Paused for the best part of the COVID-19 pandemic (where it was used for first COVID models design)

→ Re-started last year

Project Aims

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- To systematically review mathematical models, parameter values, and historical outbreaks for all listed pathogens, excluding disease X:
  - CCHF
  - Ebola
  - Lassa fever
  - Marburg virus disease
  - MERS
  - Nipah and henipaviral diseases
  - Rift valley fever
  - SARS
  - Zika

- To collate information enabling rapid mathematical modelling of these 9 pathogens including:
  - model structures
  - fatality ratios
  - reproduction numbers
  - risk factors (severity & transmission)
  - mutation rates
  - seroprevalence
  - historical outbreaks

Project organization

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Who has been involved:

- A group of ~20 volunteer researchers interested in outbreaks
- No dedicated funding nor anyone’s main project

Project outputs

- A database storing all the information extracted – *R package epireview* https://github.com/mrc-ide/epireview
  - designed to be easily updated with new info (new parameter estimates / new pathogens)

- A series of papers (anticipated):
  - 9 disease specific papers

    1 on Marburg recently published: Cuomo-Dannenburg et al. Lancet ID 2023 https://doi.org/10.1016/S1473-3099(23)00515-7

    interest in principle from Lancet family to consider all papers in several subjournals
  - 1 overview paper comparing the pathogens
    - Archetype pathogens according to their characteristics
    - Facilitating the classification of novel pathogens against these “archetypes”

  + potentially some indirectly related papers (including on recommendations for model and parameter reporting)

  + conferences posters (ASTMH, Epidemics)

Search strategy
(search initially performed in 2019)

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- We searched in OVID Medline, Embase and Web of Science:
- **Marburg** *AND (virus OR disease)* AND ((transmission OR epidemiology) OR (model* NOT imag*) OR (“burden” OR “severity” OR “case fatality ratio” OR “CFR”) OR (“serial interval” OR “incubation period” OR “generation time”) OR (“heterogeneity” OR “superspread*”) OR (“reproduction number” OR "reproductive number" OR "R0") OR (“pre-existing immunity” OR “serological” OR “serology” OR “serosurveys”) OR (diagnostic OR diagnosis OR test*) OR ("evolutionary rate" OR "genetic mutation" OR evolution) OR (outbreak OR cluster OR epidemic) OR (“risk factor*”) OR (“case definition”))

- *(adapted with other pathogen names)*
- For Marburg only we added *terms* to exclude Marburg city

It has been a lot of work!

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	title and abstracts	full text	data extraction
CCHF	1967	656	247
Ebola	9563	1277	420
Lassa	1760	322	102
Marburg	2707	190	42
MERS	10382	623	179
Nipah	959	148	58
RVF	3341	418	149
SARS	11918	800	347
Zika	4518	238	144
total	47115	4672	1688

+ updated searches

+ update of epireview

+ analyses

+ write up

Marburg virus disease (MVD): state of the scientific knowledge

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The New York Times

New Marburg Outbreaks in Africa Raise Alarm About the Deadly Virus's Spread

- 2 outbreaks in Equatorial Guinea and Tanzania last year
- But <500 cases ever reported on as of spring 2023

→ Large knowledge gaps

Cuomo-Dannenburg et al. Lancet ID, in press
https://github.com/mrc-ide/epireview

Marburg virus disease (MVD): state of the scientific knowledge

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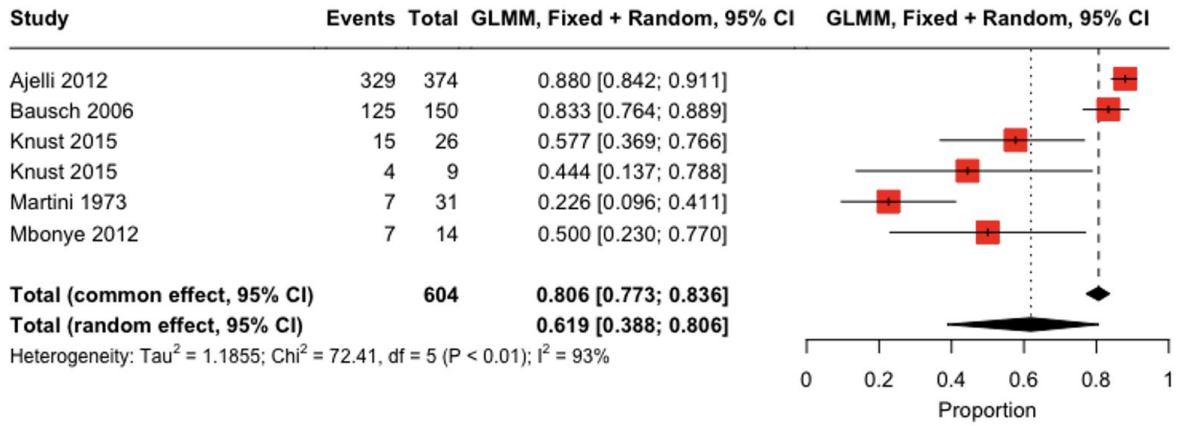
The New York Times

New Marburg Outbreaks in Africa Raise Alarm About the Deadly Virus's Spread

- Only 1 MVD mathematical model ever published
- Transmission and natural history poorly characterized.
- Case fatality ratio (% of cases who die) is high overall, ~62%, especially in large outbreaks where it can be> 80%
- More information from recent or future outbreaks can be added to our database, *epireview,* when available
- This resource will be crucial to develop mathematical models to support monitoring and intervention design in the early stages of future MVD outbreaks.

- 2 outbreaks in Equatorial Guinea and Tanzania this year
- But <500 cases ever reported on as of spring 2023

→ Large knowledge gaps

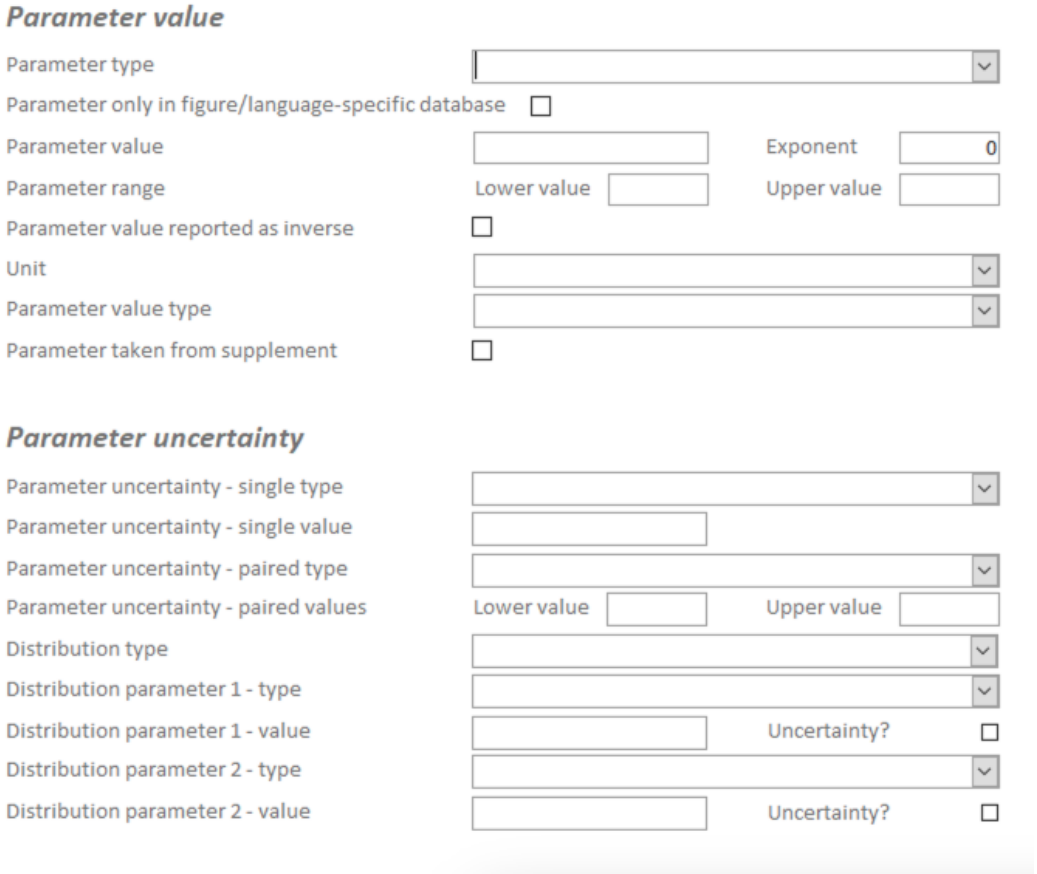


Cuomo-Dannenburg et al. Lancet ID, in press

https://github.com/mrc-ide/epireview

Key challenges and take-home messages

- Lack of standardized formats in reporting models and parameters challenging
  - We designed a dedicated access database to extract information in varied formats (available here: https://github.com/mrc-ide/epireview/blob/main/miscellaneous_files/)
  - Database being adjusted to solve issues faced during extraction of papers on Ebola



- Hard to harmonise / synthetise information reported in different formats
  - Epiverse R package epiparameters https://github.com/epiverse-trace/epiparameter a first step but not comprehensive
  - An important output of our work may be to make recommendations on best practice for reporting

Key challenges and take-home messages

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- Contextual information is important but even less standardized in reporting
  - e.g. age of the population, setting, case definition used, …

- Balance between feasibility and comprehensiveness
  → Depending on specific objectives, difference balance needed
  → Example: risk factors
    →Heterogeneity in definition of groups & reference group (in addition to outcome)
    →We decided to NOT collect any quantitative information,
    →Only collecting: what factors have been considered + significant or not + uni or multivariable

- Our rationale:
  → A user could always go back to the original paper to know more
  → Although not really compatible with real-time use

Key challenges and take-home messages

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- We focused on the **information available early on in an outbreak**, not so much on how to sustain information during an epidemic
  - → WHO Collaboratory interested in making it more general to cover that aspect too
  - → Questions around how to filter the “adequate quality” information

- We excluded grey literature

- We designed a quality assessment questionnaire generic enough to cover most aspects of modelling (given wide scope of project)

Theme	Question
Is the methodological/statistical approach suitable? (how the data are used)	1. Clear and reproducible 2. Robust and appropriate for the aim [subjective criteria]
Are the assumptions appropriate? (input parameters/assumptions - what goes into the methodology)	3. Clear and reproducible 4. Justified (published study or analysis of data)[objective criteria]
Are the data appropriate for the selected methodological approach?	5. Clearly described and reproducible 6. Are issues in data clearly discussed and acknowledged? 7. Are issues in data accounted for in chosen methodological approach?

→ Remphasises the need to design
- recommendations on best practice for reporting
- simple quality assessment schemes

Ongoing work, future plans & links with other projects

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- **Systematic review**
  - Continue our systematic review and series of papers

- **epireview R package**
  - https://github.com/mrc-ide/epireview
  - Will populate epireview with collated info on 1 pathogen at a time when papers are ready
  - See Sangeeta's talk

- **Link with LSHTM / Epiverse**
  - Packages with similar aims (epiparameter) & others that could be used in a pipeline (e.g. serofoi)
    - Approaches are very different (breadth vs depth)
    - Discussing how to align functionalities, formats etc – hackathon in March 2024

- **Link with WHO Hub collaboratory**
  - Shared experience, decisions made, extraction database template
  - Future workshops to see how our work can be used by teams working on other pathogens

Discussion / questions

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And thanks to the team (not all pictured in photo…)