

THE LANCET

Digital Health

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: McAndrew T, Majumder MS, Lover AA, et al. Early human judgment forecasts of human monkeypox, May 2022. *Lancet Digit Health* 2022; published online July 7. [https://doi.org/10.1016/S2589-7500\(22\)00127-3](https://doi.org/10.1016/S2589-7500(22)00127-3).

Appendix

Contents

Author Contributions: p2

Background: p2-3

Methods: p3-5

Forecast solicitation/collection: p5-10

Quantile predictions of transmission: p10-11

Public health impact: p12

Limitations to human judgment forecasting: p12-13

Concluding remarks: p13

References: p13-15

TRIPOD Checklist: p15-19

Ground truth as of July 1, 2022: p20

Author Contributions

TM contributed to data analysis, visualization, and manuscript preparation

MM contributed to manuscript preparation

AL contributed to visualization and manuscript preparation

SV contributed to manuscript preparation

PB contributed to manuscript preparation

TB contributed to analysis and manuscript preparation

AC contributed to visualization and manuscript preparation

DB contributed to manuscript preparation

GD contributed to manuscript preparation

SA contributed to manuscript preparation

SC contributed to data collection, data analysis, and verification

NB contributed to data analysis, verification, and manuscript preparation

JC contributed to data collection and manuscript preparation

Background

Monkeypox is a zoonotic infection caused by an orthopoxvirus and is related to the virus that causes smallpox (*Variola virus*) [1]. There are two clades of monkeypox virus: the Central African clade, which has an estimated case fatality rate of 10.6% (68/640), and the West African clade has an estimated case fatality rate of 3.6% (9/247) [2]. The monkeypox virus spreads through contact with body fluids, monkeypox lesions, contaminated items, or through respiratory droplets [3]. Primary infections in humans occur from direct contact with animal reservoirs, and past work has suggested that the most likely animal reservoir for the MPXV is rodents—though this is not confirmed [4], [5].

A unique aspect of these current clusters is apparent human-to-human transmission in non-endemic countries. An outbreak where limited human-to-human transmission occurs is not uncommon in endemic countries. The most recent outbreak where human-to-human and animal-to-human transmission occurred was in Nigeria in 2017/2018. From Sept 22, 2017 to Sept 16, 2018, the West African clade of the MPXV caused 122 confirmed or probable cases and 7 deaths across 17 states in Nigeria [6]. As of yet, there is little evidence to suggest that MPXV will cause widespread, long-term community transmission in countries outside Central and Western Africa, where MPXV has been

endemic. Instead, the virus may quickly spread and then die out, similar to past outbreaks of SARS (2003) and Nipah [7], [8]. Recent estimates, using air travel data, of the risk of importation of an infected individual from Portugal, Spain, the United Kingdom, and Canada to another country are especially high for countries where cases have already been effectively detected. [9]

In Zaire (Central African strain), the probability of household transmission from one human to another was previously estimated to be 3% (69/2278) [10]. However, there may be many factors that could contribute to an increase in transmission of the current MPXV compared to past estimates, such as decreased vaccination against orthopoxviruses since the eradication of smallpox in 1980 and spread in specific subpopulations who may have a higher number of close contacts that are suitable for transmission.

Preliminary phylogenetic analysis of sequenced genomes indicates that the ongoing multi-country outbreak is likely the result of a single introduction event and that the MPXV driving this current outbreak is closest to the West African clade of MPXV that caused the outbreak in Nigeria in 2018 [11]. This current MXPV diverges by a mean of 50 single nucleotide polymorphisms from the 2018 viruses, which may partially explain the scale of the current outbreak.

The first outbreak in the US was in 2003 but at that time no human-to-human transmission was reported, although limited evidence suggests potential asymptomatic transmission in health care settings [12]. Two more travel-related cases were identified in the USA [4] in 2021, but did not lead to secondary infections. This most recent outbreak of MPXV is the first in the US where imported infections with subsequent, human-to-human transmission is likely [3]. Local human-to-human transmission is suspected in the United Kingdom and within the European Union (EU) [13], [14].

Methods

Recruitment and solicitation

Forecasters who subscribe to Metaculus—who were not necessarily subject matter experts—were offered the opportunity to submit forecasts for questions related to MPXV. No specific material was sent to solicit participation from the Metaculus community of forecasters, however Metaculus did post the above questions on Twitter.

Unlike a typical survey, forecasters on Metaculus are given explicit, quantitative feedback on their forecasting performance in terms of both accuracy and calibration. Thousands of Metaculus forecasters participate on the platform monthly. In a 2020 survey that asked Metaculus forecasters “Which of the following reasons for visiting Metaculus do you agree with?”, the top three responses were: “enjoyment

and fun,” “training myself to think more rigorously about the future,” and “learning about fascinating topics. Forecasters on Metaculus are often standing members of a community who are dedicated to producing accurate, calibrated forecasts.

We sent personal emails on May 20, 2022 to more than 200 subject matter experts and posted solicitations to two infectious disease forecasting communities: The Modeling of Infectious Disease Agent Seminar (MIDAS), which has approximately 250 members, and the US COVID-19 Forecast hub google group, which has approximately 300 members (See supplementary information for the message sent). We estimate the total number of solicitations sent to unique experts to be more than 400. Though there are many expert solicitations, we cannot confirm the number of experts who have submitted predictions to the platform.

We define an expert as an individual who self-identifies as an expert in the modeling of infectious disease, epidemiology, or public health. The individuals that we contacted typically earned a graduate degree in the above three fields or a related field and spanned both industry and academia.

Forecast submission

A forecaster on the Metaculus platform can submit a predictive density f as a convex combination of up to five logistic distributions

$$f(x) = \sum_{k=1}^5 \pi_k g(x | \mu_k, s_k)$$

$$g(x | \mu, s) = \exp(-(x - \mu)/s) / s(1 + \exp(-(x - \mu)/s))^2$$

where π_k is a nonnegative weight associated with the k^{th} logistic distribution $g(x | \mu_k, s_k)$ and all weights are constrained to sum to one. By default, a forecaster is presented with a single logistic density and a slider bar underneath this density that contains a square and two circles (See supplemental figure). A forecaster can change the value of μ by shifting the square to the left for lower values and to the right for higher values. The parameter s is adjusted by sliding the circles left and right. If they wish, a forecaster may press “add a component” to add a second logistic distribution. A second slider will appear under the first and two additional sliders that control the weights (π) associated with the first and second logistic distribution. The predictive density a user creates is continually updated in the browser to facilitate building their forecast for submission. When the forecaster is satisfied with their prediction, they press “submit”.

After the first submission, a forecaster may revise their original prediction as many times as they choose.

Forecasters construct a predictive density over a bounded interval that is presented either on a linear scale or on a log scale (base 10). The choice of interval and linear vs. log scale is made by question developers at Metaculus.

After 10 predictions from 10 unique forecasters are submitted to the Metaculus platform, an ensemble of these predictions is revealed to the community.

Ensemble algorithm to combine individual predictions

An ensemble predictive density f was created as a weighted combination of all M individual forecaster densities

$$f(x) = \sum_{m=1}^M \pi_m f_m(x)$$

where the weight assigned to forecaster m , annotated as π_m , is a function of the forecaster's accuracy on past questions where they submitted a prediction with ground truth available and how recently they submitted a prediction. This ensemble strategy applies to questions that ask a forecaster to submit a predictive density over a closed interval. For binary questions, where forecasters are asked to submit a single probability, the ensemble strategy takes the median of all submissions.

Forecast evaluation

When the ground truth t is available, we will assess an ensemble forecast f using two different methods: (i) the difference between the truth t and median prediction and (ii) the logarithmic score.

The logarithmic score (log score) is defined as the natural log of the predicted probability density (f) value assigned to the eventually realized truth (t)

$$LS(t, f) = \log[f(t)]$$

The log score approaches negative infinity as the probability a forecast assigns to the truth approaches zero. The maximum (best) log score is a value of positive infinity. The log score is a proper score which awards predictive densities that attempt to match as close as possible the assumed probability distribution that is used to generate observed data [15].

Forecast solicitation/collection

Email solicitation sent to subject matter experts

There has been a recent reported increase in monkeypox infections in countries such as the US and Europe where the disease is not endemic. As of 20 May at 4PM EST there have been a total of 146 suspected and confirmed cases of monkeypox in countries where the disease is not typically found and

on 20 May, 2022 the World Health Organization hosted a Strategic and Technical Advisory Group meeting on the monkeypox outbreak.

To support public health decision making about the transmission and burden of the virus, we have launched a human judgment forecasting effort to aggregate probabilistic predictions about the trajectory of the monkeypox virus.

As an expert in public health, epidemiology, the modeling of infectious disease, and/or virology we ask that you take time to submit probabilistic forecasts for the following questions through the Metaculus platform as soon as possible:

- Transmission
 1. [Total estimated monkeypox infections in 2022](#)
 2. [Total monkeypox cases in Europe as of 1 July](#)
 3. [Total monkeypox cases in USA as of 1 July](#)
 4. [Total monkeypox cases in Canada as of 1 July](#)
 5. [How many countries will confirm at least one case of monkeypox by 31st July 2022?](#)
 6. [Number of US states with monkeypox cases on July 1, 2022](#)
- Public health policy and decision making
 1. [WHO declares that monkeypox is a PHEIC](#)

Metaculus is a free browser-based platform for collecting crowdsourced predictive densities of targets of interest. A forecast is composed of a convex combination of up to five logistic distributions or a binary yes/no question. Predictions can be submitted and revised as many times as you wish. Details about forecast submission can be found here <https://www.metaculus.com/help/faq/#howpredict>

Please feel free to send these questions to colleagues and close contacts who you feel too are experts in the fields of public health, epidemiology, the modeling of infectious disease and virology.

We also ask that you volunteer your name and affiliation to lend credence to these ensemble forecasts and acknowledge your time and effort to improve public health decision making. Please use the following link to add this information: https://lehigh.co1.qualtrics.com/jfe/form/SV_6lK94vY8Nyhohr8

We plan to incorporate these predictions in a manuscript and submit them for publication so that we can send, as fast as possible, rapid information about the evolving monkeypox virus. Those who choose to volunteer their name and affiliation in the above link will be included in a table of experts who contributed predictions to this work. Individual predictions will be de-identified.

Thank you for helping us in this effort to attempt to support public health decision making with rapid human judgment forecasts of the transmission and burden of the monkeypox virus.

Please feel free to send any questions about this effort to mcandrew@lehigh.edu

Thomas McAndrew

Assistant Professor

College of Health at Lehigh University

Juan Cambeiro, Nikos Bosse, Tamay Besiroglu, Sylvain Chevalier, Gaia Dempsey

Metaculus Team

Metadata related to questions posed to crowd

API url	title	Num. of Forecasts	Lower bound	Upper bound	Created time	Publish time	Resolve time
https://www.metaculus.com/api2/questions/10976/	How many human infections of monkeypox will be estimated to have occurred before 2023, worldwide?	281	200	500,000,000	2022-05-19T15:34:16.890047Z	2022-05-18T04:00:00Z	2023-12-31T20:00:00Z
https://www.metaculus.com/api2/questions/10978/	What will be the total number of confirmed and suspected	20	75	100,000	2022-05-19T16:20:34.116855Z	2022-05-19T19:00:00Z	2022-07-01T16:00:00Z

	monkeypox cases in Europe as of July 1, 2022?						
https://www.metaculus.com/api2/questions/10979/	What will be the total number of confirmed and suspected monkeypox cases in the United States as of July 1, 2022?	26	1	100,000	2022-05-19T16:39:04.867290Z	2022-05-19T19:00:00Z	2022-07-01T16:00:00Z
https://www.metaculus.com/api2/questions/10975/	How many countries will confirm at least one case of monkeypox by July 31, 2022?	82	7	196	2022-05-19T14:07:10.757688Z	2022-05-19T19:00:00Z	2022-07-31T16:00:00Z
https://www.metaculus.com/api2/questions/10981/	How many states in the United States will report having a	65	1	50	2022-05-19T18:14:38.738737Z	2022-05-19T19:00:00Z	2022-07-01T16:00:00Z

	case of monkeypox as of July 1, 2022?						
https://www.metaculus.com/api2/questions/10977/	Will WHO declare the spread of monkeypox a Public Health Emergency of International Concern before 2023?	147	0	1	2022-05-19T15:34:23.359907Z	2022-05-19T19:00:00Z	2023-01-01T17:00:00Z
https://www.metaculus.com/api2/questions/11039/	What will be the total number of confirmed and suspected monkeypox cases in Canada as of July 1, 2022?	9	22	20,000	2022-05-20T20:07:55.240251Z	2022-05-20T21:00:00Z	2022-07-01T16:00:00Z
https://www.metaculus.com/api2/questions/	How many deaths due to monkeypox	56	1	5,000,000	2022-05-19T20:03:23.195382Z	2022-05-19T22:00:00Z	2023-12-31T20:00:00Z

10982/	will be estimated to have occurred before 2023, worldwide?						
--------	--	--	--	--	--	--	--

Supp. Table 1: A line list for each question of the API url, title of the question, the number of forecasts submitted, lower and upper bounds, the creation, publication, and resolution dates.

Background information

Recently, there have dozens of reported cases of monkeypox outside of areas in sub-Saharan Africa (namely, Nigeria, Central African Republic, Cameroon, and Democratic Republic of Congo) in which it is endemic. As of 12PM EST on 19 May, there are 22 confirmed or suspected monkeypox cases across the UK, Portugal, Spain, Canada, Sweden, Italy, and the US. According to a 19 May report by the the European Centre for Disease Prevention and Control, many of these cases are likely the result of community transmission since many do not appear to be linked to travel.

Given the unusually high frequency of human-to-human transmission observed in this event, and the probable community transmission without history of traveling to endemic areas, the likelihood of further spread of the virus through close contact, for example during sexual activities, is considered to be high. The likelihood of transmission between individuals without close contact is considered to be low.

Monkeypox is closely related to but distinct from smallpox, which was eradicated in 1980. The first case of monkeypox was diagnosed in 1970 and in recent years the frequency and geographic distribution has increased in Central Africa and West Africa. A recent systematic review finds that monkeypox has a less severe clinical presentation and is less transmissible than smallpox, but also that it has been evolving in recent decades to become of "global relevance." The same article also reports a pooled case fatality rate estimate of 8.7%, with a point estimate of 10.6% for the Central African clade and 3.6% for the West African clade. As of 18 May, all sequenced monkeypox cases seem to be of the West African clade according to WHO.

In high-resource settings, the case fatality rate of the West African clade of monkeypox may be lower than 1%.

Question

How many deaths due to monkeypox will be estimated to have occurred before 2023, worldwide?

Resolution criteria

In the last week of December 2023, Metaculus admin and community moderators will review a portion of credible scientific estimates published in the year 2023, of the cumulative total number of deaths due to monkeypox that occurred in the year 2022. Admin and community moderators may decide to resolve this question on the basis of the median estimate considered they consider most credible, or decide to resolve this question as the median of all median estimates found by reviewing a portion of credible scientific literature.

If estimates of the total number of worldwide deaths are not available at the time of resolution, which may be possible in the scenario in which the global impact of monkeypox is limited, then we will resolve this by using total confirmed-suspected+possible death counts.

Also see this question on the total number of monkeypox infections in 2022.

Comments

4 comments

enter comment

Forecast Timeline

Past consensus prediction

Make a Prediction

Prediction tool

Logistic Dist. 1

Logistic Dist. 2

"Add component" option to add up to five logistic distributions

	My Prediction	Community
lower 25%	855	133
median	2.4k	332
upper 75%	10k	1.8k
> 5M	4%	1%

Supp. Fig. 1: Example of the Metaculus platform used by forecasters to generate probabilistic predictions of questions posed about monkeypox.

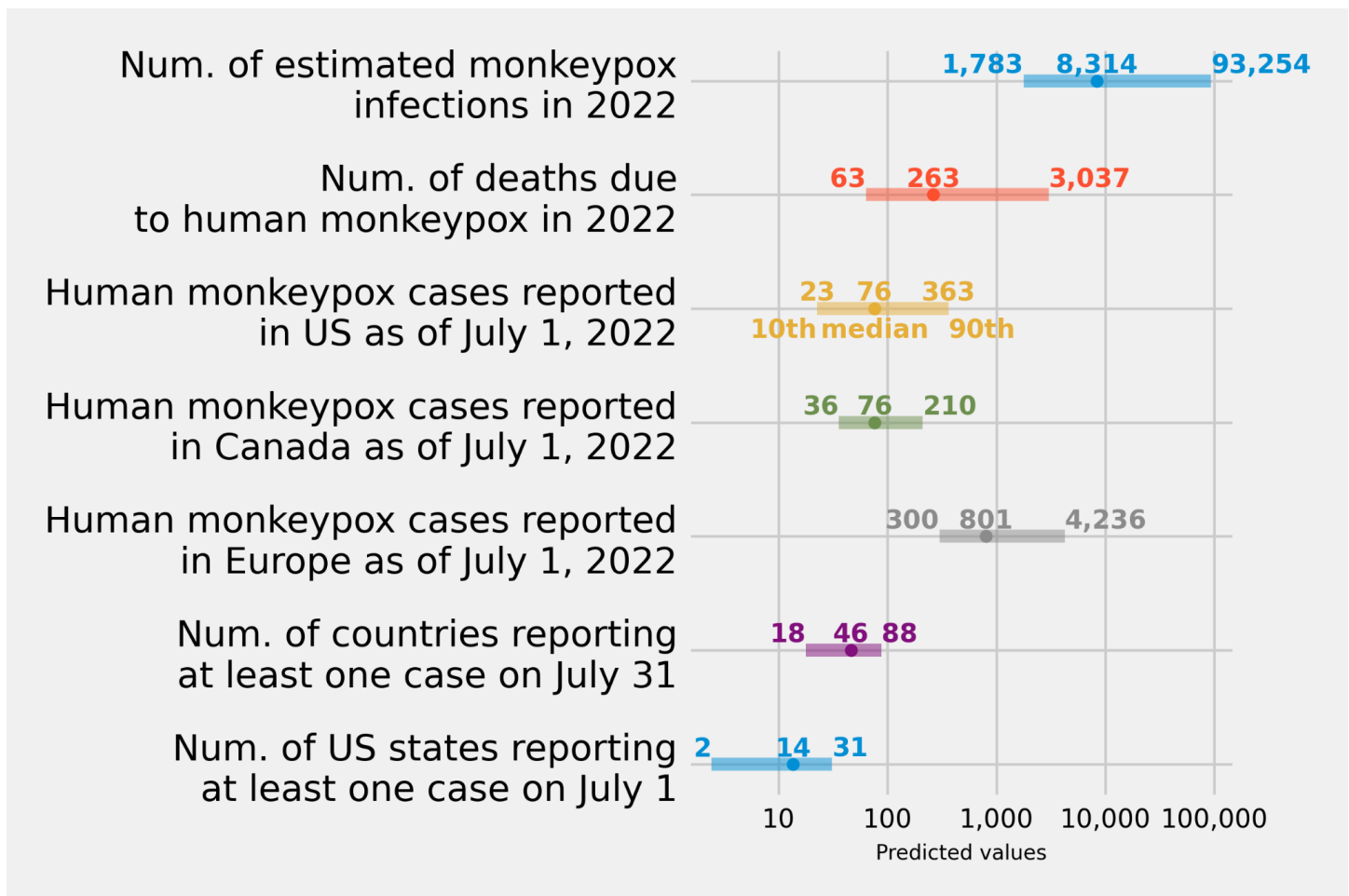
Quantile predictions of transmission

As of May 24, 2022, The crowdsourced median prediction of the estimated number of human monkeypox infections that will occur globally by the end of 2022 is 8,314 [10th percentile: 1,783, 90th percentile:

93,254]. The median prediction of the number of deaths due to human monkeypox during the year 2022 is 263 [10th percentile: 63, 90th percentile: 3,037] (Supp. Fig. 2).

The median prediction of the number of monkeypox cases by July 1, 2022 in the US is 76 [10th percentile: 23, 90th percentile: 363], in Canada by July 1, 2022 is 76 [10th: 36, 90th: 210], and in Europe is 801 [10th: 300, 90th: 4,236]. The total number of reported confirmed plus suspected monkeypox cases as of May 24, 2022 worldwide is 270, in the US is 7, in Canada is 27, and in Europe is 234.

The ensemble median prediction of the number of countries that will report one or more cases of the monkeypox infection by July 31, 2022 is 46 [10th: 18, 90th: 88]. As of May 24, 2022, the number of countries reporting one or more cases of monkeypox is 19. The median prediction of the number of states in the US that will report one or more cases by July 1, 2022 is 14 [10th: 2, 90th: 31], and as of May 24, 2022 there are 3 states reporting one or more human monkeypox cases.



Supp. Fig. 2: Quantiles from human judgment ensemble predictions for 7 questions about the monkeypox virus and human monkeypox disease. The median is represented as a circle and the shaded region captures the 10th-90th percentile of predictions.

Public health impact

At the time of publication, crowdsourced ensemble forecasts regarding the monkeypox virus suggest that reported cases will increase globally over the coming weeks. However, the crowd assigned a wide uncertainty to the reported number of cases at the global and country/region specific level, which may reflect the lack of historical data in locations outside of Sub-Saharan Africa. Relatively little weight was assigned to extremely high incidences by the ensemble forecast, indicating limited belief that monkeypox is a pandemic-level threat at this time. The crowd is also at this time uncertain about whether the WHO will declare the ongoing outbreak a Public Health Emergency of International Concern (PHEIC). That said, the crowd assigned a median probability close to 25% that the virus is declared PHEIC. The median probability the crowd assigned to a PHEIC started at 80% and decreased to approximately 25%, indicating that forecasters have revised their predictions over time to align with new information about the outbreak.

Current crowd predictions suggest that the existing smallpox vaccine emergency stockpiles (2.8 million in Geneva; ca. 600 million globally) are likely sufficient for ring vaccination of close contacts, but that many countries should proactively plan for extensive demands on health systems for contact tracing, and quarantine/isolation spaces [16].

A forecasting platform offers an approach for rapidly aggregating predictions from statistical models, mechanistic models, and intuition. Independent infectious disease modeling teams may not have a streamlined process for sharing forecasts and modeling approaches with one another, or teams may have limited motivation to do so. A forecasting platform like the one presented here supports, and incentivises, the sharing of computational forecasts and human intuition and expertise. Finally, a forecasting platform can serve as a repository for current forecasts—both computational and intuition-based—of targets of public health importance. Limitations to human judgment forecasting are detailed in the appendix

Limitations to human judgment forecasting

Limitations of human judgment forecasting are a lack of transparency into how predictions are formed; limits placed by the forecasting platform on the shape of a predictive density, as well as the choice of scale (linear vs. log)—both of which may bias predictions; that resolution criteria for questions may not be clear; that the wording of each question may bias forecasters, and the fact that any subscriber, not just those with expertise in modeling, can submit predictions [17]. The Metaculus platform allows forecasters to submit, alongside their prediction, comments such as the data they used to form a prediction or what

techniques they used when making their predictions. However, submitting a comment is not required, which makes it difficult to more fully examine the factors incorporated into a submitted forecast. Forecasters on the platform are constrained to submit predictions over a bounded interval that is determined a priori and forecasters are limited to a set of five logistic distributions for submission. The platform also a priori restricts predictions to be submitted on a linear scale or a logarithmic scale. This choice of scale could put undue influence on how a forecaster produced their prediction. An additional limitation is that questions posted on the platform must be accompanied by a resolution source. Thus questions that need answering must wait until a suitable resolution source can be identified, and adapted when better sources become available. Finally, Metaculus, like many forecasting platforms, places minimal restrictions on who can submit a forecast. Although trained ensembles based on forecasters' past performance can be employed, performance on questions unrelated to infectious disease may not apply to predictions of the monkeypox outbreak. Because of the above limitations, we caution trusting the above—or any probabilistic forecast of the future.

In addition, how the Metaculus crowd estimates risks may be skewed by observing, and predicting, events that are unrelated to the spread of a pathogen such as economic and politic events, and pathogens that have dissimilar characteristics to the MPX outbreak such as seasonal influenza, and the COVID-19 pandemic

We could not conclude whether any experts that were contacted submitted forecasts, and as of May 24, 2022 zero experts have included their name and affiliation alongside a forecast. A challenge to address for the future is development of (1) trust between experts and the forecasting community and (2) methods to motivate experts to participate. Experts could share valuable insights that may not only improve an ensemble prediction, but improve the knowledge of individual, non-expert forecasters. Future work should also address to what degree forecasters are influenced by observing the ensemble forecast and current reported data.

Concluding remarks

Human judgment probabilistic predictions can be rapidly mobilized to support public health decision making during an outbreak when the infrastructure required for them is in place and sufficiently robust. They are flexible enough to incorporate changing public health needs during the course of an outbreak and can complement traditional computational approaches with the use of qualitative expert opinion.

References

- [1] L. Khodakevich, Z. Ježek, and D. Messinger, "Monkeypox virus: ecology and public health

significance,” *Bull. World Health Organ.*, vol. 66, no. 6, pp. 747–752, 1988.

[2] E. M. Bunge *et al.*, “The changing epidemiology of human monkeypox—A potential threat? A systematic review,” *PLoS Negl. Trop. Dis.*, vol. 16, no. 2, p. e0010141, Feb. 2022, doi: 10.1371/journal.pntd.0010141.

[3] “Monkeypox in the United States | Monkeypox | Poxvirus | CDC,” Nov. 19, 2021. <https://www.cdc.gov/poxvirus/monkeypox/outbreak/us-outbreaks.html> (accessed May 19, 2022).

[4] “Update: Multistate Outbreak of Monkeypox --- Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003.” <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a5.htm> (accessed May 22, 2022).

[5] “Human monkeypox: an emerging zoonotic disease | Future Microbiology.” <https://www.futuremedicine.com/doi/abs/10.2217/17460913.2.1.17> (accessed May 22, 2022).

[6] “Outbreak of human monkeypox in Nigeria in 2017–18: a clinical and epidemiological report - The Lancet Infectious Diseases.” [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(19\)30294-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30294-4/fulltext) (accessed May 22, 2022).

[7] N. S. Zhong *et al.*, “Epidemiology and cause of severe acute respiratory syndrome (SARS) in Guangdong, People’s Republic of China, in February, 2003,” *The Lancet*, vol. 362, no. 9393, pp. 1353–1358, Oct. 2003, doi: 10.1016/S0140-6736(03)14630-2.

[8] N. I. Paton *et al.*, “Outbreak of Nipah-virus infection among abattoir workers in Singapore,” *Lancet Lond. Engl.*, vol. 354, no. 9186, pp. 1253–1256, Oct. 1999, doi: 10.1016/S0140-6736(99)04379-2.

[9] “Monkeypox - MOBS Lab.” <https://www.mobs-lab.org/monkeypox.html> (accessed May 23, 2022).

[10] Z. Ježek, B. Grab, M. V. Szczeniowski, K. M. Paluku, and M. Mutombo, “Human monkeypox: secondary attack rates,” *Bull. World Health Organ.*, vol. 66, no. 4, pp. 465–470, 1988.

[11] “Multi-country outbreak of Monkeypox virus: genetic divergence and first signs of microevolution - Monkeypox,” *Virological*, May 23, 2022. <https://virological.org/t/multi-country-outbreak-of-monkeypox-virus-genetic-divergence-and-first-signs-of-microevolution/806> (accessed May 23, 2022).

[12] A. T. Fleischauer *et al.*, “Evaluation of human-to-human transmission of monkeypox from infected patients to health care workers,” *Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am.*, vol. 40, no. 5, pp. 689–694, Mar. 2005, doi: 10.1086/427805.

[13] “Monkeypox - United Kingdom of Great Britain and Northern Ireland.”

<https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON383> (accessed May 22, 2022).

[14] “Multi-country monkeypox outbreak in non-endemic countries.”

<https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385> (accessed May 24, 2022).

[15] A. H. Murphy and R. L. Winkler, “Probability Forecasting in Meteorology,” *J. Am. Stat. Assoc.*, vol. 79, no. 387, doi: 10.1080/01621459.1984.10478075.

[16] “Smallpox eradication: destruction of variola virus stocks,” p. 5.

[17] B. C. K. Choi and A. W. P. Pak, “A Catalog of Biases in Questionnaires,” *Prev. Chronic. Dis.*, vol. 2, no. 1, p. A13, Dec. 2004.

TRIPOD Checklist

Section/Topic		Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	1
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	Page 1 Lines 60-71
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	Lines 52-59
Methods			

Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	Lines 52- 59
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	Page 1 Lines 72- 73
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	NA
	5b	Describe eligibility criteria for participants.	Page 6 Lines 222- 235
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	Page 1 Lines 52- 59 and Page 9 Lines 320- 323
	6b	Report any actions to blind assessment of the outcome to be predicted.	NA

Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	Page 7 Lines 256- 274
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	Page 6 Lines 222- 235
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	Page 7 Lines 236- 274
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	Page 7 Lines 256- 274
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	Page 7 Lines 265- 274
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			

Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	NA
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	Page 6 Lines 222-235
Model development	14a	Specify the number of participants and outcome events in each analysis.	Page 1 Lines 72-73
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	NA
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	Page 7 Lines 236-274
	15b	Explain how to use the prediction model.	
Model performance	16	Report performance measures (with CIs) for the prediction model.	Not available
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	Page 12 Lines 370-388

Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	Page 2 Lines 105- 115
Implications	20	Discuss the potential clinical use of the model and implications for future research.	Page 11 and 12 Lines 348- 369
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	Page 3 Lines 116- 121
Funding	22	Give the source of funding and the role of the funders for the present study.	Page 5

Ground truth as of July 1, 2022

Prediction target	Location	Value	Source	Date of report
Number of reported cases	Worldwide	3413	World Health Organization*	June 27, 2022
Number of reported cases	European Union	2933	World Health Organization*	June 27, 2022
Number of reported cases	United States	142	World Health Organization*	June 27, 2022
Number of reported cases	Canada	210	World Health Organization*	June 27, 2022
Number of countries to report ≥ 1 infection	Worldwide	50	World Health Organization*	June 27, 2022
Number of US states to report ≥ 1 infection	United States	30	Centers for Disease Control and Prevention**	July 1, 2022
WHO Declaration of PHEIC	NA	No	World Health Organization***	June 25, 2022

* [https://www.who.int/emergencies/disease-outbreak-news/item/2022-](https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON396#:~:text=Since%201%20January%20and%20as,new%20countries%20have%20reported%20cases.)

[DON396#:~:text=Since%201%20January%20and%20as,new%20countries%20have%20reported%20cases.](https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON396#:~:text=Since%201%20January%20and%20as,new%20countries%20have%20reported%20cases.) ** <https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html> ***

[https://www.who.int/news/item/25-06-2022-meeting-of-the-international-health-regulations-\(2005\)-emergency-committee--regarding-the-multi-country-monkeypox-outbreak](https://www.who.int/news/item/25-06-2022-meeting-of-the-international-health-regulations-(2005)-emergency-committee--regarding-the-multi-country-monkeypox-outbreak)