[Name of the institution and name of the administrative unit] [case number]

Institution: UiO

Administrative unit: IMB

Title of case study: Models for the management of the covid pandemics in Norway

Period when the underpinning research was undertaken: 2015-2022

Period when staff involved in the underpinning research were employed by the submitting

institution: 2015-2022

Period when the impact occurred: 2020-2023

1. Summary of the impact

OCBE's research has been essential for the management of the covid pandemic in Norway. From the very start of the pandemic, we have developed and run our mathematical and statistical models to (1) estimate the reproduction number R in each region of Norway, (2) to perform prediction of the number of hospitalised covid patients; and (3) to perform what-if studies on the efficacy of interventions (vaccines, lockdown and re-opening strategies ...). Our results were regularly used by the National Institute of Public Health (NIPH), the Health Directorate, hospitals, national and local governments, to take key decisions. During the pandemic, OCBE and NIPH had a joint modelling team constantly on duty, also responsible for communication with the public (weekly reports) and the media. Norway's handing of the pandemic is recognised as very successful, and this is also thanks to our contribution.

2. Underpinning research

State-of-the-art by 2015: Stochastic compartmental metapopulation models were known to be useful for situation awareness, forecasting and scenario simulation in epidemics. Informed by multiple sources of data (incidence of cases, hospital admissions), they allow to quantify the strength of viral transmission (reproduction number R), to estimate the number of infected individuals, and to predict the future number of infected and of hospitalized patients. *Individual-based models* were known as mathematical representation of an interacting population, with their demography and transmission networks in different social layers (households, schools, workplaces).

Our contribution per 2019: OCBE and NIPH, within our sfi BigInsight, had projects and PhD students in models for epidemics, which turned out to be essential for our Covid work:

- R1. We developed a new spatio-temporal stochastic model for the spread of an infection based on mobile phone mobility and a sequential Approximate Bayesian Computation (ABC) for efficient inference. (2019 PhD Solveig Engebretsen, then started at Norsk Regnesentral (NR).)
- R2. We developed an individual-based model, reproducing the Norwegian population's sociodemography, representing households, hospitals and nursing homes, calibrated to 2008–2015 and applied to MRSA bacteria. (2019 PhD Francesco Di Ruscio, started at NIPH.)

Our contribution during the Covid pandemic 2020-2022: Already in February 2020, OCBE, NIPH, NR and Telenor formed the Oslo Covid-modelling group. Throughout the pandemic, our relentless efforts, built on expertise and new scientific findings, allowed us to produce essential modelling results for Norway. Below, key methods developed during this period, which were in daily use and turned out to be powerful instruments for epidemic management for Norway:

- We extended R1 to Norway, using the Norwegian Telenor mobile phone mobility data (updated every six hours during the whole pandemics).
- Real-time inference was crucial, with data arriving on Monday mornings and results required by Wednesday mornings. Existing algorithms couldn't handle time-piecewise constant reproduction numbers (changing every 2-3 weeks). To address this, we created a novel

sequential ABC, named split-seqABC, enabling efficient use of our stochastic metapopulation models with a high parameter count.

- Daily changing reproduction numbers are more precise than time-piecewise constant reproduction numbers. We developed a new model with daily-varying reproduction number, to quantify the viral transmission in real time. We proposed a state-space formalisation of the model and a sequential Monte Carlo approach which also runs in real-time.
- Throughout the COVID years, we routinely received specific inquiries from the government and others, involving decisions on optimal interventions. To address these what-if scenarios, we enhanced our individual-based model R2, dividing Norway into 13,521 cells, each with the actual population. The model incorporated various age-structured contact routes, such as community, household, school, and workplace, utilizing Telenor mobility data. This refined model proved instrumental in guiding decisions, including optimizing vaccination strategies and post-Omicron lockdown reopening. It stands as the most advanced individual-based model for Norway, surpassing the level of detail found in comparable models, such as the UK ones.
- In addition, we produced results on specific aspects of covid epidemiology, which had impact on the management of the pandemics. For example:
 - We compared Omicron's epidemic growth to Delta's, using December 2021 January 2022 contact tracing data. We found increased Omicron susceptibility despite three-dose vaccination, with infected individuals efficiently spreading the virus, while three-dose vaccinated contacts had lower infection risk.
 - We criticised for major shortcomings in design and methodology, a randomised trial on Covid transmission in fitness centres in Oslo, suggesting that these were not a place of special spread.
 - We established an international multidisciplinary research group to develop a questionnaire for patients with or after covid disease, including long-covid, to assess their health-related quality of life. The questionnaire has been used in many clinical studies, and for example help to conclude that Baricitinib should not be used to treat Covid patients.

Our contribution after the Covid pandemic: We continue publishing our methods and findings, to document our work and to prepare for future pandemics. For example, our analysis revealed that mandating recommendations to reduce contacts did not result in fewer contacts compared to just recommendations. Consequently, less intrusive and costly non-mandatory measures may prove effective in Norway in the future.

Funding: BigInsight, NFR, Nordforsk; In-kind: UiO, NIPH, Telenor, NR; Supercomputing: UiO, Sigma2.

- Oslo Covid-modelling group, included:
- Birgitte Freiesleben de Blasio NIPH and OCBE (20%) (leader)
- Arnoldo Frigessi OCBE (leader)
- Francesco Di Ruscio OCBE (PhD) and NIPH
- Solveig Engebretsen OCBE (PhD) and NR.
- Chi Zhang OCBE (PhD) and NIPH.
- David Swanson (OCBE)
- Contributors from OCBE in additional activities:

Jon Michael Gran, Marissa Erin LeBlanc, Morten Valberg, Corina Silvia Rueegg, Ragnhild Sørum Falk

3. References to the research

Engebretsen, S., Engø-Monsen, K., Aleem, M.A., Gurley, E.S., Frigessi, A. and De Blasio, B.F., 2020. Time-aggregated mobile phone mobility data are sufficient for modelling influenza spread: the case of Bangladesh. *Journal of the Royal Society Interface*, 17(167), p.20190809.

Di Ruscio, F., Guzzetta, G., Bjørnholt, J.V., Leegaard, T.M., Merler, S. and De Blasio, B.F., 2019. Quantifying the transmission dynamics of MRSA in the community and healthcare settings in a low-prevalence country. *Proceedings of the National Academy of Sciences*, 116(29), pp.14599-605.

Engebretsen, S., Diz-Lois Palomares, A., Rø, G., Kristoffersen, A.B., Lindstrøm, J.C., Engø-Monsen, K., Kamineni, M., Hin Chan, L.Y., Dale, Ø., Midtbø, J.E. and Stenerud, K.L., Di Ruscio, F., White, R., Frigessi, A., De Blasio, B.F., 2023. A real-time regional model for COVID-19: Probabilistic situational awareness and forecasting. *PLOS Computational Biology*, *19*(1), p.e1010860.

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Jalali, N., Brustad, H.K., Frigessi, A., MacDonald, E.A., Meijerink, H., Feruglio, S.L., Nygård, K.M., Rø, G., Madslien, E.H. and De Blasio, B.F., 2022. Increased household transmission and immune escape of the SARS-CoV-2 Omicron compared to Delta variants. *Nature Communications*, *13*(1), p.5706.

Kamineni, M., Engø-Monsen, K., Midtbø, J.E., Forland, F., de Blasio, B.F., Frigessi, A. and Engebretsen, S., 2023. Effects of non-compulsory and mandatory COVID-19 interventions on travel distance and time away from home, Norway, 2021. *Eurosurveillance*, 28(17), p.2200382.

Günther, F., Brustad, H.K., Frigessi, A. and Britton, T., 2024. Quantifying the impact of social activities on SARS-CoV-2 transmission using Google mobility reports. Submitted to PNAS, available on *medRxiv*.

Valberg, M., Gran, J. M., Rueegg, C. S., & LeBlanc, M. (2022). Letter to the editor regarding "Covid-19 transmission in fitness centers in Norway-a randomized trial". <u>BMC public health</u>, 22(1), 1-2.

4. Details of the impact

OCBE was a founder and key part of the Oslo Covid-modelling group: key scientific results originated from OCBE, De Blasio and Frigessi were joint leaders of the group, with their ex-PhD students fully active. The impact was during the whole pandemic (2020-2022) and continues today in terms of preparedness for future pandemics. We were part of the NIPH pandemic management during the whole period, with responsibility for all modelling and predictions. The groups included about 15 researchers, including system and data engineers and epidemiologists, in addition to us statisticians. We were responsible for all methodology and algorithms, including weekly runs. Typically, our week started Monday at 8 am, when we froze the current data and started running our models, with results ready on Wednesday morning, when the report was prepared and submitted at 12:00. The modelling group had a meeting on Monday at 8:00 to decide what algorithms to run, on Wednesday to discuss results and on Friday to critically discuss and decide about needed improvements and planning the specialised reports, with hard work all week long, often including weekends: week after week, taking turns during vacations. In addition, we were responsible for communication with the public and media on all modelling and prediction. Meetings were also organised with health authorities that used our results and regularly with all the Nordic health authorities.

Our results reached immediately the health authorities and the government. The R-number was used in the public discourse, including uncertainties in estimating it. We experienced several times to hear the minister or the health directors to cite from our reports during press conferences on tv, just few hours after publication.

It is difficult to quantify the impact of our results. We dare to say that the beneficiaries is the whole Norwegian population, in terms of lives saved, reduced hospitalisation and illness, increased economical benefits. Norway as a country, has been able to manage the pandemics well, citing from the national <u>Coronavirus Commission</u>: "The country's population and its authorities have

handled the pandemic well overall. Norway has had one of Europe's lowest mortality rates, least restrictive infection control regimes and smallest declines in economic activity." One reason for this is the timeliness with which the national and the local governments have introduced interventions, to prevent the spread to explode. Our estimates and predictions were making this possible.

In order to give evidence of the importance of our work, we cite (our translations) from the report of the Coronavirus Commission, "Evaluering av pandemihåndteringen - Rapport fra Koronautvalget, 29. april 2022, for å gjennomgå og trekke lærdom fra koronapandemien i Norge", see section 12.3.5 on "Matematisk infeksjonsmodellering": "The situational understanding included mathematical modelling to estimate the disease burden of the epidemic in the coming weeks. Mathematical infection modelling was part of a comprehensive knowledge base, and NIPH's professional advice was always provided based on a holistic assessment. - By quantifying health loss and the burden of measures, the [modelling] group could highlight the societal consequences of reducing imported infections, differentiating measures geographically, or illustrating how characteristics of the virus variant influenced the choice of strategy. - Throughout the pandemic, projections of infection numbers, hospitalizations, and sick leave were crucial parts of the government's decision-making basis. The committee believes that such projections have clear utility as decision-making tools and should, therefore, be used in future crises." The report in section 12.3.5 also includes two statements, here translated: Prime Minister Støre described his relationship with the models and that these results were useful in "challenging decision-makers to consider what to do with hospital capacity ... that must be scaled up if [the predictions would] materialize." Espen Nakstad, Assistant Director of the Norwegian Directorate of Health, said on the role of models and predictions: "It has probably influenced political decisionmakers, both locally and nationally, especially to see alarming models. It is important to say. But we have contributed to seeing it not as forecasts but possible scenarios. In that sense, I don't think it has always been very decisive."

In addition, we believe that a further impact of our work, of more long term and educational type, is the increased understanding by the general population of uncertainty quantification of predictions. We think that recognising the presence of uncertainty in decision making, can more generally help to increase the trust in government and politics – important in our current world.

OCBE also participated (with JM Gran) to the national commission responsible for deciding whether to stop the use of the Astra-Zeneca vaccine.

Mistakes we did in the covid period also made an impact, not only our correct results: we failed to explain well enough the assumptions of our three-week ahead predictions. These were such that we predicted the number of new covid hospitalisations, given that no new intervention would be implemented, and given that the population would continue to have the same mobility. Aftenposten, the main Norwegian newspaper, found that our predictions were pessimistic when the spread was increasing, and this was the main news on 15 June 2021. The reason for this difference was that when our predictions were alarming, then governments often would introduce additional restrictions and people would naturally behave more carefully, thus leading to less hospitalisations than predicted. We tried to explain this, but it was difficult.

Finally, we mention possible long term impacts of our work: We are preparing scientific papers which use the Norwegian and Nordic data to explain if and how interventions were useful, with the hope to increase knowledge for future situations. We mention that while NIPH had to cut their staff significantly, their modelling team was not reduced, recognising the importance of our work.

5. Sources to corroborate the impact

Weekly reports *Situational awareness and forecasting for Norway,* published from 14.4.2020 until 25 may 2023 (Tidligere publiserte rapporter):

https://www.fhi.no/ss/korona/koronavirus/koronavirus-modellering/

An example is here, for 24 November 2022:

https://www.fhi.no/contentassets/e6b5660fc35740c8bb2a32bfe0cc45d1/vedlegg/nasjonale-ogregionale-rapporter/2022-11-24-national regional model 22.pdf

The NIPH published also a weekly report which always included a summary of our results, which then were seen in a global perspective ("Alle ukerapporter 2020-2023", in Norwegian) https://www.fhi.no/publ/statusrapporter/luftveisinfeksjoner/#alle-ukerapporter-2020-2023

Example of report prepared to answer a specific question of the government, here on the possible vaccination of children between 12 and 15 years (in Norwegian), 26 August 2021: https://www.fhi.no/contentassets/3596efb4a1064c9f9c7c9e3f68ec481f/2021-09-02-oppdrag-45 vedlegg-2 modelleringsrapport rettet.pdf

Example of report where modelling was a major component: Socio-economic assessment, 15 February 2021, see for example tables V.1 and V.7, among many results from our models: https://www.fhi.no/contentassets/3596efb4a1064c9f9c7c9e3f68ec481f/2021-09-02-oppdrag-45 vedlegg-2 modelleringsrapport rettet.pdf

Example of impact of our quality-of-life questionnaire, to stop using a certain treatment: https://www.helsedirektoratet.no/veiledere/koronavirus/vaksiner-smittevernutstyr-og-legemidler/legemiddelbehandling-behandling-av-covid-19/bruk-av-baricitinib-olumiant

Selection from the media (in Norwegian):

- Into the Unknown, Klassekampen, 17 March 2020: https://klassekampen.no/utgave/2020-03-17/inn-i-det-ukjente
- The FHI expert does not think we will get the R-number below 1 again, NRK, 24 march 2021, https://www.nrk.no/norge/fhi-ekspert-tror-ikke-vi-far-r-tallet-under-1-igjen-1.15431839
- Aftenposten makes mistakes on forecasts. Again and again. Aftenposten, 18 June 2021, https://www.aftenposten.no/meninger/kronikk/i/7KbAKo/aftenposten-bommer-om-prognoser-igjen-og-igjen, answer to the article on Aftenposten of 15 June 2021: https://www.aftenposten.no/norge/i/0KLBLG/prognosene-bommet-fullstendig-paa-antallet-pasienter-igjen-og-igjen
 - Posted on social media (17.000 impressions; Frigessi had 1500 followers during the pandemics) https://x.com/freeges/status/147259646686386186?s=43
- More recently: Mandates during the pandemic had a greater effect in large cities, Finansavisen, 1 may 2023, https://www.finansavisen.no/samfunn/2023/05/01/8004900/pabud-under-pandemien-hadde-storre-effekt-i-store-byer?zephr sso ott=Oq3Qk7
- In English: COVID-19: The Norwegian model, The UNESCO Courier, 15 December 2022, https://courier.unesco.org/en/articles/covid-19-norwegian-model

During the pandemic, we gave many ZOOM presentations, including for example:

- Alan Turing Institute, London, 17 March 2022: https://www.turing.ac.uk/people/guest-speakers/arnoldo-frigessi
 https://www.turing.ac.uk/events/probabilistic-approach-situation-awareness-and-forecasting-covid-19-pandemics-norway
- Data Science in the Post-Covid World, University of Helsinki, 11 May 2021
 https://www.helsinki.fi/en/faculty-science/news/hidata-webinar-data-science-post-covid-world-11-may-2021

"Evaluering av pandemihåndteringen - Rapport fra Koronautvalget, oppnevnt ved kongelig resolusjon 29. april 2022 for å gjennomgå og trekke lærdom fra koronapandemien i Norge" https://www.regjeringen.no/contentassets/b1dace9390054c85a5a87c7bbf1bc384/no/pdfs/nou202320230016000dddpdfs.pdf

Camilla Stoltenberg, director of NIPH, thanks BigInsight for the work during Covid times, in Norwegian, subtitled; her video is the first linked in this page:

https://www.biginsight.no/news/2023/11/21/biginsight-celebration-day-was-fun