

Institution: Imperial College London		
Unit of Assessment: 10 – Mathematical Sciences		
Title of case study: B10-6 Statistical Inference of Vaccine Coverage and Confidence		
Period when the underpinning research was undertaken: 2015-2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Prof Nick S Jones (NJ) Dr Alexandre de Figueiredo (AF)	Role(s) (e.g. job title): NJ: Professor of Mathematical Sciences AF: PDRA in the EPSRC Centre for the Mathematics of Precision Healthcare, Dept of Mathematics	Period(s) employed by submitting HEI: NJ: 2011 – date AF: 6/2016-11/2016, 6/2017-11/2017, 2018-2020
Period when the claimed impact occurred: 2015-2020		
Is this case study continued from a case study submitted in 2014? N		
<h3>1. Summary of the impact</h3> <p>The World Health Organisation (WHO) recently listed vaccine confidence as a top-ten global threat (WHO Global Threats 2019). Imperial research on vaccine coverage and confidence directly led to changes in national vaccine policy, resulting in increased vaccinations and reduced levels of infection. Consequent on NJ/AF's 2016 research, the Wellcome Trust and the EU commissioned, in collaboration with the team, influential world-wide and European surveys (2018, 2019). Further, the WHO commissioned NJ/AF in 2019 to improve their vaccine coverage analytic and predictive methodologies. NJ/AF's work, presented to a French Commission in 2016, and appearing in its report, directly influenced the French health minister to increase the number of state-required vaccines in France (which came bottom in the team's estimate of its level of safety-trust in 2016). The number of state-required vaccines consequently more than tripled after 2017: in 2018 alone, this led to >350,000 additional vaccinations and significant drops in infections, notably an 83% drop in invasive meningococcal infections in infants.</p>		
<h3>2. Underpinning research</h3> <p>Context: NJ's research group, in the Department of Mathematics at Imperial, has investigated vaccine coverage and confidence since 2014, in collaboration with anthropologists in the London School of Hygiene and Tropical Medicine (Prof Heidi Larson). Mathematically, this research is an adjunct to NJ's work on spreading, inference and influence on social graphs. <i>Vaccine coverage</i> is the proportion of individuals that should be vaccinated that are, in fact, vaccinated. <i>Vaccine confidence</i> indicates the level of trust in vaccine importance, safety and efficacy; hence it captures the reluctance or refusal to be vaccinated despite the availability of vaccines. A lack of vaccine coverage can then be attributed to the combination of vaccine availability and the level of vaccine confidence. NJ and AF have contributed significantly to the quantification of both vaccine coverage and vaccine confidence.</p> <p>Work on Vaccine Coverage: NJ/AF developed an analysis of factors underpinning international variations in vaccine coverage and then combined this with Gaussian-Process based forecasts of future vaccine coverage [1]. Due to this work, NJ/AF were commissioned by the WHO in 2019 to update their vaccine coverage analytics. Using a Bayesian hierarchical framework and Gaussian Processes, AF/NJ have extended the WHO's existing platform to allow coverage forecasting and inferences for countries with missing or sparse data [2].</p> <p>Work on Vaccine Confidence: The work on vaccine coverage [1] led on to work on vaccine confidence. In [3], NJ/AF analysed a large-scale survey on international vaccine confidence that</p>		

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their team collected. In addition to carrying out a large part of the interpretation of the data, NJ/AF studied covariation between responses and developed a hierarchical model to link personal and country-level predictors to survey responses. This model highlighted several actionable points; in particular, the ambiguous role that education has on improving vaccine confidence, where countries with a higher mean level of education have more negative vaccine sentiments, and the fact that gender has a mild role on vaccine safety confidence. Both factors were discussed by the French consultation '*Concertation Citoyenne sur la Vaccination*' (see below).

The paper [3] led the EU (Directorate General for Health and Food Safety) and the Wellcome Trust to commission EU and worldwide surveys, respectively. AF influenced the survey design, which followed on the design developed in [3] and carried out the analysis of these surveys while he was a Research Fellow in the EPSRC Centre for the Mathematics of Precision Healthcare (NJ – co-I). This work led to an EU report [4] which used a similar analysis as in [3]. Further, AF has produced a recent Lancet paper presenting the Wellcome Trust survey [5] which extends the statistical methodology used in [2] by incorporating multinomial logit Gaussian Processes.

3. References to the research

- [1] de Figueiredo A, Johnston IG, Smith DM, Agarwal S, Larson HJ, Jones NS, 2016, Forecasted trends in vaccination coverage and correlations with socioeconomic factors: a global time-series analysis over 30 years. *Lancet Global Health*. 4:e726-e735, [doi:10.1016/S2214-109X\(16\)30167-X](https://doi.org/10.1016/S2214-109X(16)30167-X).
- [2] de Figueiredo A, Jones NS, 2020, Gaussian Process Estimates of National Immunisation Coverage. WHO internal report.
- [3] Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, Cook AR, Jones NS, 2016, The State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey. *EBioMedicine*. 12:295-301, [doi: 10.1016/j.ebiom.2016.08.042](https://doi.org/10.1016/j.ebiom.2016.08.042).
- [4] Larson HJ, de Figueiredo A, Karafillakis E, Rawal M, 2018, The State of Vaccine Confidence in the EU 2018. https://ec.europa.eu/health/sites/health/files/vaccination/docs/2018_vaccine_confidence_en.pdf
- [5] de Figueiredo A, Simas C, Karafillakis E, Patterson P, Larson HJ, 2020, Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study. *Lancet*. 396:898-908, [doi:10.1016/S0140-6736\(20\)31558-0](https://doi.org/10.1016/S0140-6736(20)31558-0).

4. Details of the impact

Impact in France:

The work of NJ/AF in [3] led to a member of their team being called before a French national commission (the '*Concertation Citoyenne sur la Vaccination*', see below) [A] to report their findings. Combined with press coverage of [3], this testimony led to the commission issuing a report that *resulted in the French Ministry of Health substantially increasing the number of state-required vaccinations and so markedly reducing numbers of infections*.

In September/October 2016, there was a '*Concertation Citoyenne sur la Vaccination*' in France (initiated by the health minister). This citizen consultation had two committees: one composed of medics and the other composed of the public. Heidi Larson, the joint first author (with AF -- Imperial) of [3], was called as a witness (8 Sept 2016) to the medical committee and presented the team's results one day before they were released online. The transcript of this extensive presentation can be found in [A, p262-268] of which the below is an excerpt:

"Madame LARSON –...the timing is very good ... tomorrow we will be releasing an e-biomedicine in 67 countries on vaccine confidence. You are the headlines. ... France ... was, not by a small margin, the absolute least confident country in vaccine, particularly safety, but also its effectiveness. ..."

Monsieur FISCHER, President. - Thank you very much, this was really a performance. A lot of information, not good for us, but, at least, it is a further reinforcement that the work of our group is more than needed. There is a lot to do everywhere in the world, but, unfortunately mostly in France."

The (medical) committee then went on to discuss details of the breakdown of opinions expressed by survey respondents in [3], including by gender, and asked for the analysis in NJ/AF's paper itself. (See [A] p268).

Paper [3] was subsequently reported on in two articles in Le Monde [B], had coverage in La Tribune, and remains heavily referenced in the French (Le Monde, L'Express) and international media [J].

The report produced by the French commission, "Rapport sur la Vaccination" (30/11/2016 [C]) cites paper [3] in its opening paragraphs (p5), in particular stressing the high levels (41%) of vaccine hesitancy (i.e., low confidence) in France. In fact, the majority of the document covers vaccine confidence (rather than merely vaccine coverage). The consultation recommended that all childhood vaccinations be made mandatory (state-required).

On 5 July 2017, the French Health Minister announced the extension of mandatory vaccination, explicitly citing the consultation [D]. Refs [E, F] explain how the minister addressed the committee's principal recommendation (i.e., mandatory vaccination) as a direct consequence of report [C]. A recent analysis [G] of the effects of this mandatory vaccination (which cites paper [3] and its follow-up for the EU [4]) stated:

"...the extension of vaccination mandates on vaccination coverage is encouraging. It shows an increase in VC [Vaccine Coverage] of infants concerned by the extension of the vaccination mandates ... vaccine coverage for the first dose of meningococcal C vaccine increased from 39.3% to 75.7% ... This sharp increase in MenC VC translated into a dramatic decrease in the number of invasive MenC disease cases notified in infants through the mandatory notification system"

Ref. [4] further notes that the number of invasive Meningococcal infections dropped six-fold in one year: from 3 per 100,000 (infants <1 year) in 2017 to 0.5 in 2018. MMR vaccine coverage levels increased by 3% in 2017/18 (MMR is a key vaccine for public health and target for concerns regarding vaccine safety). The number of HPV vaccines paid for increased by ~120,000 from 2016/17 to 2018 (from ~30,000 to ~40,000 per month).

NJ/AF's work thus directly led to changes in French Vaccination policy, in vaccines delivered, and in infections averted. After French steps to increase mandatory vaccination, Germany recently passed a law that made measles vaccinations mandatory from March 2020 [H].

Impact on WHO:

NJ/AF's track record on vaccine analytics enabled them to win support to improve the WHO's reporting of coverage [2]. As a consequence of their efforts the WHO are developing probabilistic estimates of coverage [I]. WHO vaccine coverage estimates are highly significant since institutions like the Gates Foundation and GAVI tie their financial aid to WHO estimates of coverage levels.

Impact on EU and Wellcome Trust:

Consequent on paper [3], both the European Commission and Wellcome Trust commissioned large-scale surveys of the EU and World, respectively. These new surveys used the survey questions from the eBioMedicine paper [3] and sought to track progress from 2016. The vaccination part of the Wellcome Trust survey generated widespread media attention in its own right. Released in June 2019, it was picked up across the world (BBC/Reuters/CNN/Nature/Science and [5] is in the top 1000 of papers scored by Altmetric out of 17M).

Media Impact:

AF has shown that vaccine confidence has recently rebounded in France, with a ~25% increase in the number of French respondents strongly agreeing in vaccine safety (2015 survey compared to 2019 survey) [5]. Beyond influencing perceptions in France the work of NJ/AF [1,3-5] has

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impacted global awareness of vaccine confidence as a key issue and hence the need to tackle confidence: the research has been covered in >200 press articles in over 130 media outlets worldwide including: UK (Financial Times, Daily Mail, BBC), US (Newsweek, NYT), and European (Le Monde, El Confidencial) news, TV and Radio news (Al Jazeera, Europe 1, CNN, Fox, NPR), and online venues like Vox and The Conversation. It has also been reported widely in the generalist science journals Science, The Lancet and Nature (appearing in 1 world-view, 1 feature, 3 perspectives, 2 news items), and popular science magazines (Scientific American, New Scientist). Paper [3] is in the top ~0.01% of all papers scored all-time by Altmetric [J]. With its nearly 500 citations, NJ/AF's work is now used when people appeal to international challenges with both vaccine confidence and coverage.

5. Sources to corroborate the impact

[A] Transcript from *Concertation Citoyenne sur la Vaccination* (Quote is from p262)

<http://concertation-vaccination.fr/wp-content/uploads/2016/04/Annexes-rapport-CCV.pdf>

(Archived [here](#))

[B] French press coverage in Le Monde

https://www.lemonde.fr/medecine/article/2016/09/09/scandales-sanitaires-controverses-les-raisons-de-la-defiance-en-france-contre-les-vaccins_4995062_1650718.html (Archived [here](#))

https://www.lemonde.fr/sante/article/2016/09/09/plus-de-quatre-francais-sur-dix-estiment-que-les-vaccins-ne-sont-pas-surs_4994856_1651302.html (Archived [here](#))

[C] The report produced by the French commission, "Rapport sur la Vaccination"

<http://concertation-vaccination.fr/wp-content/uploads/2016/04/Rapport-de-la-concertation-citoyenne-sur-la-vaccination.pdf> Larson et al. 2016 paper is cited on page 5 of the report.

(Archived [here](#))

[D] The French Health Minister announcement of the extension of mandatory vaccination

<https://solidarites-sante.gouv.fr/actualites/presse/communiques-de-presse/article/a-partir-de-2018-les-enfants-de-moins-de-deux-ans-devront-etre-vaccinees-contre> (Archived [here](#)) and

<https://solidarites-sante.gouv.fr/actualites/presse/discours/article/discours-d-agnes-buzyn-relatif-a-la-vaccination-obligatoire-le-5-juillet-2017> (Archived [here](#))

[E] Lévy-Bruhl D, Desenclos JC, Quelet S, Bourdillon F., 2018, Extension of French vaccination mandates: from the recommendation of the Steering Committee of the Citizen Consultation on Vaccination to the law. *Eurosurveillance*. 26;23 (Archived [here](#))

[F] Ward JK, Colgrove J, Verger P, 2018, Why France is making eight new vaccines mandatory. *Vaccine*. 36(14):1801-3. (Archived [here](#))

[G] Lévy-Bruhl, D, Fonteneau, L, Vaux, S, Barret, AS, Antona, D, Bonmarin, I, Che, D, Quelet, S and Coignard, B, 2019, Assessment of the impact of the extension of vaccination mandates on vaccine coverage after 1 year, France. *Eurosurveillance*, 24;26. (Archived [here](#))

[H] Torjesen, I. German parliament votes to make measles vaccination mandatory. *BMJ*. 2019 367:I6558 (Archived [here](#))

[I] Letter of support – Scientist, Strategic Information Group, WHO.

[J] Combined evidence for global press coverage of Paper [3]

<https://dimensions.altmetric.com/details/11977011> and Paper [5]

<https://dimensions.altmetric.com/details/89829172> (Archived [here](#))