

Development and external validation of prediction models for critical outcomes of unvaccinated COVID-19 patients based on demographics, medical conditions and dental status

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Introduction: Multiple prediction models were developed for critical outcomes of COVID-19. However, dental status was never considered a potential predictor in the previous models. The study aimed to develop and externally validate prediction models for critical outcomes of COVID-19 for unvaccinated adult patients based on demographics, medical conditions, and dental status.

Methods: The unvaccinated adult hospitalized patients and outpatients who were diagnosed with COVID-19 between January 2020 and July 2021 from Isala Hospital Zwolle, and Northwest Clinics Alkmaar were included as derivation cohort and validation cohort, respectively. Demographics, medical conditions, and dental status were considered potential predictors. The critical outcomes of COVID-19 (i.e. death and ICU admission) were considered endpoints. Logistic regression analyses were used to develop two models: for death alone and for critical outcomes. The performance and clinical values of the models were determined in both cohorts.

Results: 285 and 352 patients were included from the two hospitals, respectively. Age, number of teeth, chronic kidney disease, hypertension, diabetes, and chronic obstructive pulmonary diseases were the significant independent predictors. The models showed good to excellent calibration with observed: expected (O:E) ratios of 0.98 (95%CI: 0.76 to 1.25) and 1.00 (95%CI: 0.80 to 1.24), and discrimination with shrunken area under the curve (AUC) values of 0.85 and 0.79, based on the derivation cohort. In the validation cohort, the models showed good to excellent discrimination with AUC values of 0.85 (95%CI: 0.80 to 0.90) and 0.78 (95%CI: 0.73 to 0.83), but an overestimation in calibration with O:E ratios of 0.65 (95%CI: 0.49 to 0.85) and 0.67 (95%CI: 0.52 to 0.84).

Conclusion: The performance of the models was acceptable in both derivation and validation cohorts. Number of teeth was an additive important predictor of critical outcomes of COVID-19. It is an easy-to-apply tool in hospitals for risk stratification of COVID-19 prognosis.

Conflicts of interest to disclose: We declare no competing interests

Association between adverse events after COVID-19 vaccination and anti-SARS-CoV-2 antibody concentrations in the VAccine Study COVID-19 (VASCO)

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INTRODUCTION: Previous studies suggested that adverse events (AE) after COVID-19 vaccination may be related to antibody concentrations. We aimed to describe AE after COVID-19 vaccination and investigate the association between AE and antibody concentrations before and after vaccination.

METHODS: Participants of an ongoing prospective cohort study (VASCO) completed a questionnaire on AE after each COVID-19 vaccination and provided 6-monthly serum samples. Data from May 3rd 2021 to November 6th 2022 were included. Logistic regression analyses were performed to investigate determinants, including pre-vaccination anti-RBD Ig antibody concentrations, of AE after mRNA COVID-19 vaccination. Multivariable linear regression, stratified by dose, was performed in SARS-CoV-2 naïve participants to assess the association between AE and log-transformed antibody concentrations 3-8 weeks after mRNA vaccination.

RESULTS: In total, 48,079 AE questionnaires were completed by 28,186 participants. Overall, AE were reported in 57% of questionnaires. In 43% and 34% of questionnaires, injection site and systemic AE were reported, respectively. In 2.2% of questionnaires, participants sought medical attention due to a (suspected) AE; of these, 20% concerned fever, headache or fatigue.

AE were reported significantly more frequently by women, younger participants (<60), participants with medical risk conditions and Spikevax recipients (versus Comirnaty). Higher pre-vaccination antibody concentrations associated positively with systemic AE after the second and third but not fourth dose. AE were associated with higher post-vaccination antibody concentrations after the third dose (geometric mean concentration ratio: 1.36, 95%CI: 1.22-1.52) but not the second (1.08, 95%CI: 0.95-1.24) or fourth dose (1.10, 95%CI: 0.98-1.24).

CONCLUSION: We found several factors associated with AE after COVID-19 vaccination corresponding to previous findings. Additionally, AE were associated with pre- and post-vaccination antibody concentrations, although this was not consistent across doses. Our research adds to a body of evidence that could be helpful in managing expectations surrounding AE after COVID-19 vaccination in the general public.

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Status of onchocerciasis (river blindness) elimination in Africa: results from a systematic review

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Introduction: Onchocerciasis, caused by the parasitic worm *Onchocerca volvulus* and transmitted by black flies that breed near rivers, can lead to severe skin disease and even blindness. Mass drug administration (MDA) of ivermectin, which kills the microfilariae of the worms, as well as vector control are two ways of preventing transmission. Amid the ongoing MDA control programs that were initiated decades ago, this study aimed to assess the current status of onchocerciasis in Africa and the factors affecting its elimination.

Methods: We selected articles that reported (1) either elimination or at least 10 years of MDA and (2) at least one epidemiological assessment being conducted. We classified the disease affected areas into three: “elimination reported”, “close to elimination”, and “ongoing transmission” and performed a multivariable logistic regression to understand the roles of the factors like MDA duration, coverage, baseline microfilarial prevalence, and vector (blackfly) control.

Results: We selected 63 articles which had 231 observations from the same/different disease affected areas, with 8%, 29%, and 62% of them in the groups “elimination reported”, “close to elimination”, and “ongoing transmission”, respectively. Our preliminary regression results showed that high treatment coverage for longer durations is more associated with “(close to) elimination”, whereas high baseline microfilariae prevalence is correlated with higher chances of “ongoing transmission”.

Conclusion: MDA seems an effective strategy to achieve elimination, as it has been reported for several endemic situations, advocating MDA programs for onchocerciasis elimination.

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Lyme arthritis in the knee in a Lyme endemic area in the Netherlands

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Introduction: Little is known on Lyme arthritis in the Netherlands. Diagnostic tests are difficult to interpret. Lyme arthritis could be underdiagnosed. The study objective was to assess epidemiological characteristics and frequency of diagnostic tests in patients with mono-arthritis in a Lyme endemic area.

Methods: An observational retrospective study was performed. Patients included had mono-arthritis and were referred to the outpatient clinic of rheumatology or pediatrics of Gelre hospitals between January 2013 and December 2021. Data were retrieved from patient files. Diagnostic tests consisted of Lyme serology in blood and a PCR on synovial fluid. Lyme serology was considered positive in case of a positive or equivocal ELISA/CLIA test confirmed with immunoblot. Prevalence and incidence were calculated, as well as the frequency and outcome of diagnostic tests.

Results: In total 276 patients were included of which 64 had Lyme arthritis, 75 reactive arthritis, and 137 other types of arthritis. The prevalence of Lyme arthritis was 23% (95% CI 18 – 29). The incidence was 2.5 patients (1.9 – 3.2) per 100.000 inhabitants per year. In 70.7% (195/276) of patients Lyme serology was tested and in 32.6% (90/276) of patients Borrelia PCR was performed on synovial fluid. Of patients with Lyme arthritis all but one, had positive Lyme serology. For one patient with Lyme arthritis serology was not tested. This patient had a positive Borrelia PCR in synovial fluid. In 63.8% of patients with mono-arthritis a history of a tick bite and/or erythema migrans was asked. Of patients with Lyme arthritis, 37.5% had a history of a tick bite.

Conclusion: Almost a quarter of all mono-arthritis of the knee was caused by Lyme borreliosis. We suggest Borrelia serology in blood and Borrelia PCR in synovial fluid can be part of standard care in patients with mono-arthritis, irrespective of a history of a tick bite.

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External validation of six COVID-19 prognostic models for predicting mortality risk in older populations in a hospital, primary care, and nursing home setting

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Introduction: COVID-19 pandemic has a significant global impact particularly the older population who have a greater risk of severe illness and death. We externally validated six COVID-19 prognostic models predicting mortality risk in the older population in different healthcare settings.

Methods: Based on a living systematic review of COVID-19 prediction models, we selected six prognostic models predicting the risk of mortality in adults with a COVID-19 infection (GAL-COVID-19 mortality, 4C Mortality Score, NEWS2-extended model, Xie model, Wang clinical model, CURB65 score). The six validation cohorts (three hospital, two primary care, and a nursing home cohort) comprised of Dutch older individuals of ≥ 70 years of age with a clinical or PCR-confirmed COVID-19 diagnosis. All six prognostic models were validated in hospital setting with the GAL-COVID-19 mortality model being validated in all settings. Model performance was evaluated in each validation cohort separately in terms of discrimination, calibration, and decision curves. An intercept update was performed in models with indications of miscalibration.

Results: Results in three cohorts (one in each setting) were shown to be suboptimal, where the calibration-in-the-large ranged from -1.44 to -0.80 (0 for good calibration), calibration slope 0.24 to 1.01 (1 for good calibration), and c-statistic 0.55 to 0.71 (1 for good discrimination). Further results will be presented at the conference.

Conclusion: Our results show that the six prognostic models performed poorly in the older population in hospital, primary care, and nursing home settings. A possible explanation is that age was included as a linear term in the validated models. The suboptimal performance clarifies the need for tailoring of COVID-19 prognostic models before implementation in older populations.

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Impact of a pneumococcal polysaccharide vaccination program on invasive pneumococcal disease in elderly in the Netherlands

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Introduction: In 2020, a national program for pneumococcal vaccination in the elderly was initiated, providing the 23-valent pneumococcal polysaccharide vaccine (PPV23) to individuals born between 1941-1947, with those born between 1948-1952 being vaccinated in 2021. The uptake of the vaccine was estimated at 73%-74%. We evaluated the impact of the vaccination program on the incidence of invasive pneumococcal disease (IPD) using national surveillance data.

Methods: IPD isolates were collected and serotyped from hospital laboratories by the National Reference Laboratory of Bacterial Meningitis. We used IPD-surveillance data from September 2016 to October 2022 and used two complementary analysis methods.

Method 1 was a controlled pre-post analysis, calculating the impact as one minus the odds ratio (OR) of having IPD caused by a PPV23-serotype (VT-IPD) in vaccine-eligible cases compared to cases not (yet) eligible for vaccination, controlled for the OR during the four respiratory seasons previous to implementation (2016/2017–2019/2020).

Method 2 was a regression discontinuity analysis. We modeled the IPD-incidence by age using a Poisson model controlled for respiratory season and with an interaction term for age and vaccine-eligibility. The impact was defined as one minus the incidence rate ratio for vaccine-eligibility.

We calculated both overall estimates and estimates stratified by birth cohort and time since implementation, this abstract only presents the overall estimates.

Results: Since October 2020, 1783 IPD cases were reported among those aged 60 years and older, including 525 vaccine-eligible cases. The controlled pre-post design showed an overall impact on VT-IPD of 25% (95% CI: 3-42). The regression discontinuity analysis showed an overall impact on VT-IPD of 39% (95% CrI: 29-48) and no statistically significant impact on non-VT-IPD (21%; 95% CrI -3–44).

Conclusion: Using two models with different underlying assumptions, we showed an impact of 25-39% of PPV23 vaccination on VT-IPD in vaccine-eligible age-cohorts.

Conflicts of interest to disclose: We declare no competing interests