The Potential Clinical and Economic Benefits of Updated Omicron-Containing Bivalent SARS-CoV-2 Boosters Compared With First Generation Prototype Boosters in Germany Assuming BA.4/BA.5 Dominance

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BACKGROUND

- Several vaccines were rapidly developed and deployed in response to the coronavirus disease 2019 (COVID-19) pandemic[1]
  - Although many of these vaccines are highly effective against severe COVID-19 outcomes, waning immunity and emerging variants of concern remain a global challenge[2]
- The high prevalence of the omicron subvariants BA.4 and BA.5, in conjunction with their increased transmissibility and ability to escape vaccine-induced immunity, is a major cause for public health concern[3,4]
  - The novel mRNA-based COVID-19 vaccine from Moderna (mRNA-1273) was originally approved for primary series use by the European Medicines Agency in January 2021, and subsequently as a booster dose[5]
- Next generation omicron-specific bivalent boosters including mRNA-1273.214 (ancestral- and BA.1-specific) and mRNA-1273.222 (ancestral- and BA.4/BA.5-specific) may substantially reduce hospitalizations, deaths, and associated costs over a monovalent ancestral booster (mRNA-1273)[6,7]

OBJECTIVE

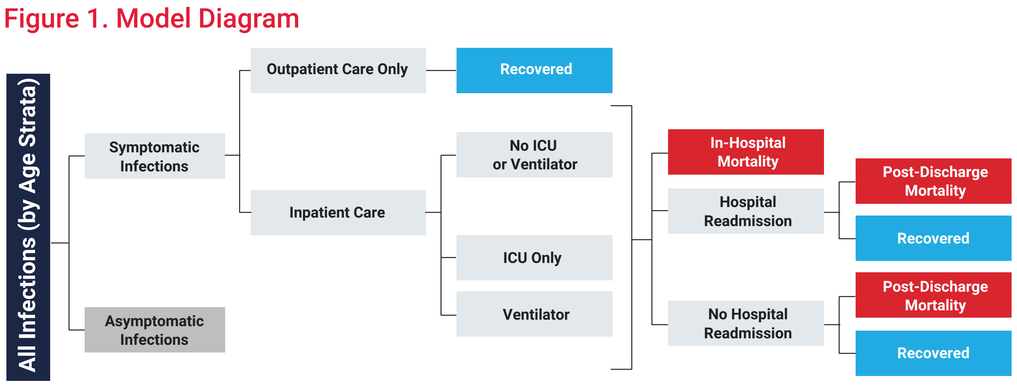
- To estimate the clinical and economic outcomes of the administration of monovalent, bivalent BA.1-specific, or bivalent BA.4/BA.5-specific boosters for adults (≥18 years) and older adults (≥60 years) in Germany over a 1-year time horizon

METHODS

Study Design

- A static decision-analytic model was developed to estimate the monthly COVID-19–related hospitalisations, deaths, and costs per 100,000 persons (age stratified to match the German general population) boosted with monovalent, bivalent BA.1-specific, or bivalent BA.4/BA.5-specific vaccines
  - Results were modelled only on individuals who completed a primary COVID-19 vaccination series
  - All booster vaccines were assumed to be delivered in September 2022
- Estimated monthly COVID-19 infections were calculated by applying booster effectiveness against infection to incidence rates in unvaccinated individuals[8]
  - Hospitalisation rates were also calculated to capture additional booster effectiveness against severe disease
- Hospitalisation rates during the period prior to vaccination were reduced by 25% to account for the lower risk of hospitalisation associated with omicron variants BA.4/BA.5, which were assumed to be the dominant variants throughout the study period[9]
- Initial vaccine effectiveness (VE) against infection and severe disease was calculated using the Khoury/Hogan model[10,11]
  - Additional detailed methods and model parameters are presented in the **Supplementary Methods and Supplementary Table 1 (accessible by scanning the QR code)**
- Infections move through the decision tree illustrated in **Figure 1**
  - Asymptomatic individuals were not included, as they have no associated direct costs
  - Only hospitalised patients were assumed to be at risk of death
- For cost calculations, vaccine costs and administration fees were not considered, as they were assumed to be equivalent for all vaccine types
  - Discounting was not applied

Figure 1. Model Diagram



ICU, intensive care unit.

RESULTS

Clinical Outcomes of Interest: Hospitalisations and Deaths

- The bivalent BA.1-specific booster is expected to reduce hospitalisations and deaths by up to 15% in both adults (≥18 years) and older adults (aged ≥60 years) compared with a monovalent booster (**Figure 2**)
- The bivalent BA.4/BA.5-specific booster is expected to reduce both hospitalisations and deaths by up to 20% compared with a bivalent BA.1-specific booster and up to 32% compared with the monovalent booster in all adults and older adults
- The results based on the sensitivity analysis (**see Supplementary Methods and Supplementary Table 1; accessible by scanning the QR code**) are shown in **Figure 3**

Figure 2. Predicted Number of (A) Hospitalisations and (B) Deaths per 100,000 Adults (≥18 Years) or Older Adults (≥60 Years) Boosted With Monovalent, Bivalent BA.1-Specific, and Bivalent BA.4/BA.5-Specific Vaccines

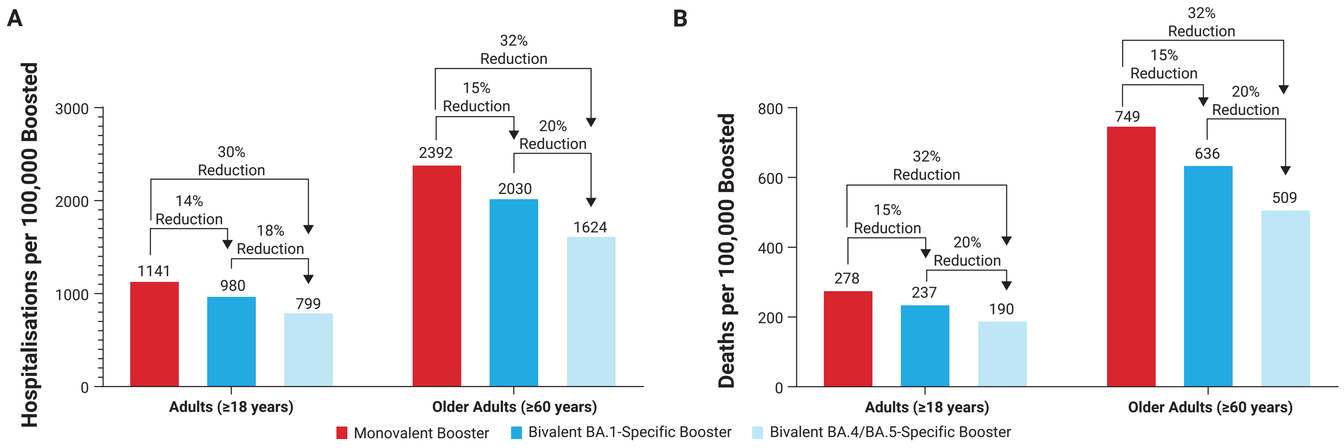
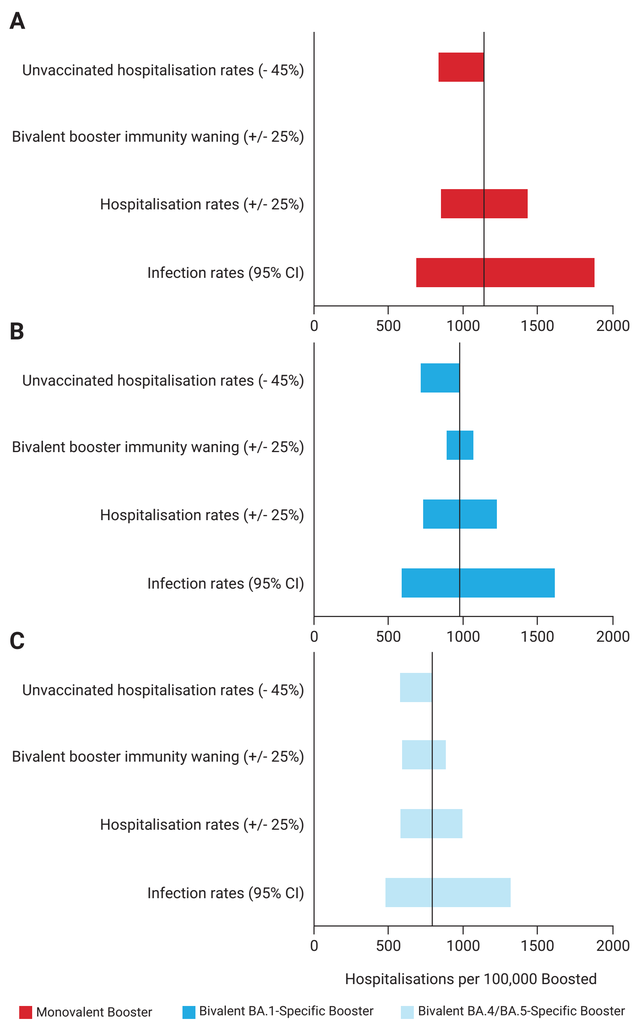


Figure 3. Estimated Hospitalisations per 100,000 Adults as Determined via Sensitivity Analyses (≥18 Years) Boosted With (A) Monovalent, (B) Bivalent BA.1-Specific, and (C) Bivalent BA.4/BA.5-Specific Vaccines

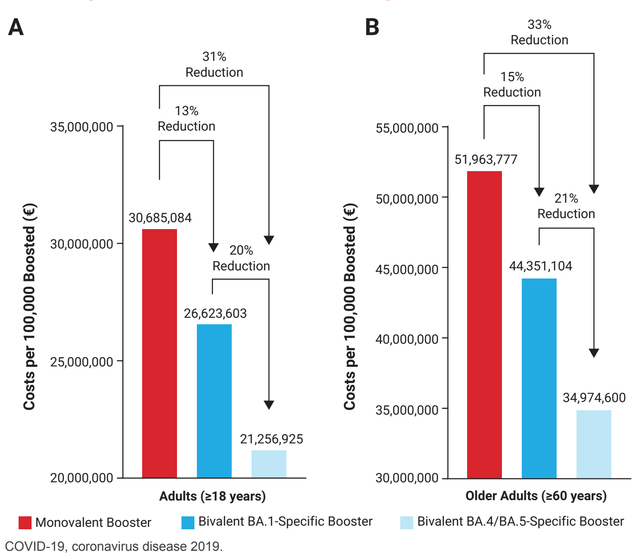


CI, confidence interval.
Vertical line represents the predicted hospitalisations for each vaccine scenario

Economic Outcomes: Treatment Costs

- Compared with the monovalent booster, the bivalent BA.1-specific booster would result in an estimated reduction of (**Figure 4**):
  - €4,061,481 per 100,000 boosted adults (aged ≥18 years)
  - €7,612,673 per 100,000 boosted older adults (aged ≥60 years)
- Compared with the bivalent BA.1-specific or monovalent boosters, the bivalent BA.4/BA.5-specific booster would result in an estimated reduction of:
  - €5,366,678 or €9,428,159 per 100,000 boosted adults (≥18 years), respectively
  - €9,376,504 or €16,989,177 per 100,000 boosted older adults (≥60 years), respectively

Figure 4. COVID-19–Related Treatment Costs per 100,000 (A) Adults (≥18 Years) and (B) Older Adults (≥60 Years) Boosted With Monovalent, Bivalent BA.1-Specific, and BA.4/BA.5-Specific Vaccines



COVID-19, coronavirus disease 2019.

CONCLUSIONS

- The broad immune responses associated with next-generation bivalent boosters are expected to avert more hospitalisations, deaths, and treatment costs than monovalent boosters, especially among older adults (≥60 years)
  - Assuming continued predominance of BA.4/BA.5 throughout the upcoming year in Germany, the bivalent BA.4/BA.5-specific booster may improve clinical and economic outcomes of COVID-19 compared with a bivalent BA.1-specific or monovalent booster over the same time period

ABSTRACT PLAIN LANGUAGE SUMMARY

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Disclosures

BU, AN, POB, and NVDV are employees of Moderna, Inc., and hold stock/stock options in the company. MK is a shareholder in Quadrant Health Economics Inc., which was contracted by Moderna, Inc., to conduct this study. MM, KF, and AL are consultants at Quadrant Health Economics Inc. BS and RC are consultants at ICON plc, which was contracted to support this study.

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