Effects of Adolescent MenACWY and MenC Vaccination in Germany: A Modelling Study

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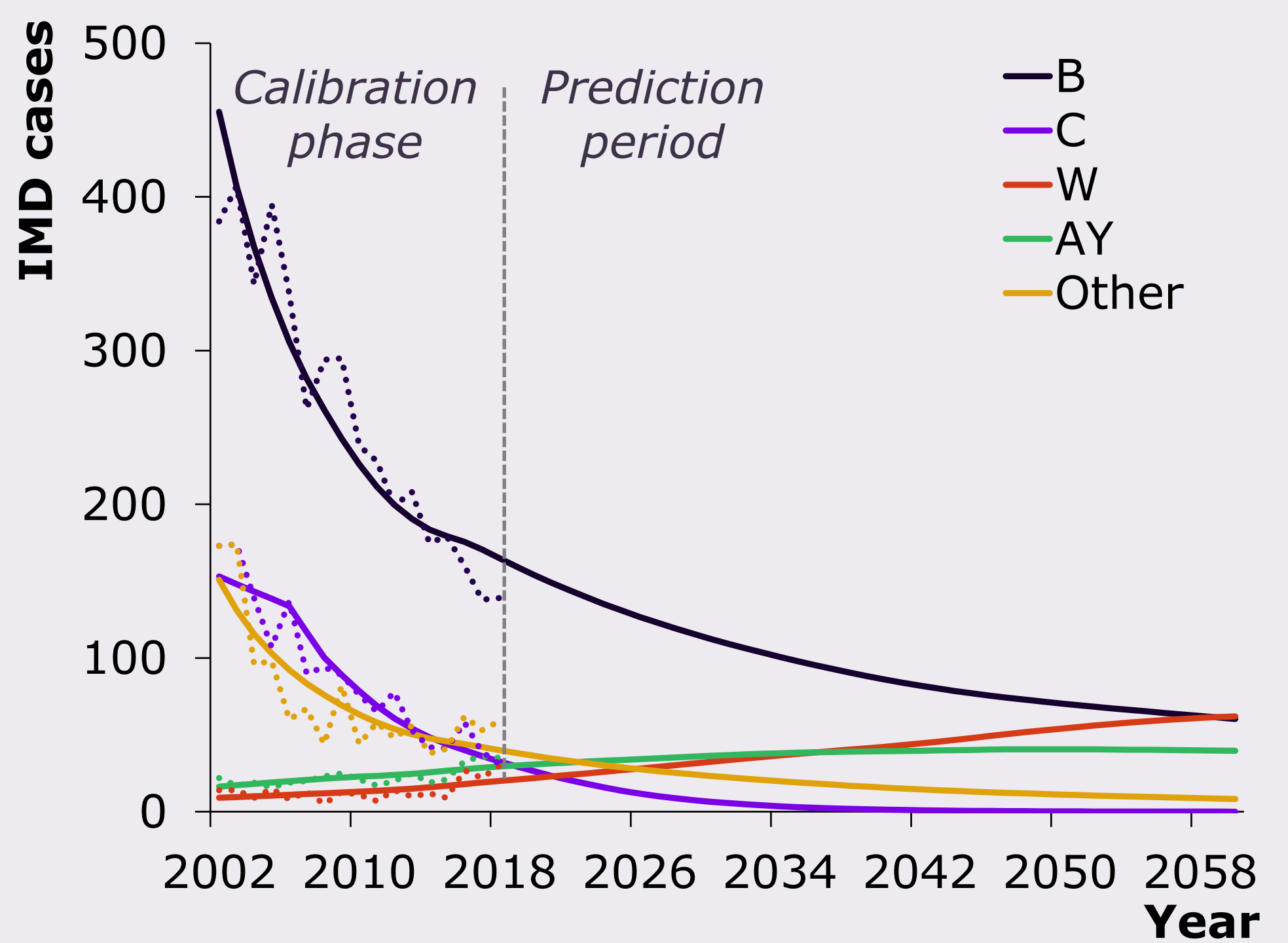
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INTRODUCTION

Invasive meningococcal disease (IMD) is a severe infection caused by *Neisseria meningitidis* (Nm), which is associated with high lethality and severe long-term sequelae in survivors. In Germany, routine vaccination against Serogroup C Nm (MenC) is recommended for toddlers at age 1 year. Protective effects wane over time and existing evidence suggests a peak of Nm carriage prevalence in adolescents.[1]

Objective

This study aims to evaluate the potential public health impact and cost-effectiveness of implementing adolescent booster strategies with MenACWY and MenC vaccines in Germany, where routine meningococcal immunization is currently limited to MenC in toddlers.

METHODS

- We constructed a Susceptible-Infected-Susceptible **(SIS) dynamic transmission model** to project meningococcal carriage of five serogroups (B/C/W/AY/Others) without competitive interaction across 100 age cohorts until 2060, with corresponding IMD cases derived using case-carrier ratios.
- In 6 scenarios (Sc), we compared the existing routine **MenC toddler vaccination** to **additional MenC or MenACWY boosters** at ages 12-14 or 15-17 years, considering vaccine effectiveness against IMD (VE) and carriage acquisition (VEc):
  - **Sc1***: MenACWY booster, age 12-14 years, VEc 36%[2]
  - **Sc2**: MenACWY booster, age 15-17 years, VEc 36%[2]
  - **Sc3**: MenACWY booster, age 12-14 years, VEc 80%[3]
  - **Sc4**: MenACWY booster, age 15-17 years, VEc 80%[3]
  - **Sc5**: MenC booster at age 12-14 years; VEc 75%[4]
  - **Sc6**: MenC booster at age 15-17 years; VEc 75%[4]
  - ******base case analysis*

- **Key input** parameters for the **transmission model**:
  - Vaccination coverage rate: 90%[5] in toddlers, 50% in adolescents (assumption).
  - VE against invasive disease: 89%[6] for ages 2-10y, 96%[7] age >10y (all-or-nothing approach).
  - Waning of vaccine-induced protection: exponential decay with average duration of 5 years in toddlers, 10 years in adolescents.[8]
  - Carriage duration: 6 months.[9]
- Leveraging the results of the transmission model, a **cost-utility analysis (CUA)**, based on a decision-tree, was conducted from a societal perspective.
- In the CUA, we applied vaccine costs of €41.89 for MenC and €44.30 for MenACWY[10], and administration costs: €8.00.[11]
- HCRU and treatment costs were extracted from a cost-of-illness study by Scholz et al. (2019).[12]

Fig. 1: Notified IMD cases and model predictions under current vaccination strategy by serogroup, 2002-2060

Dotted: observed cases; solid: model predictions

Fig. 2: a) Predicted incremental IMD cases per year by scenario; b) Cumulative no. of prevented IMD cases over the extrapolation period (2019-2060)

*base case analysis

METHODS (continued)

- We applied age- and serogroup specific case-fatality rates and considered **16 IMD-sequelae** in survivors with corresponding proportions from a recent systematic review.[13]
- To calculate quality-adjusted life-years (QALYs), health state utility values (HSUV) for the acute phase of IMD and for the potential sequelae were informed from an unpublished systematic review.
- Costs and health effects were **discounted at 3%**, and a scenario with 1% for QALY gain was explored.
- To account for societal preferences of preventing rare but devastating diseases such as IMD, a QALY adjustment factor **(QAF) of 3** was applied to QALY loss from long-term sequelae in **scenario analysis**.[14-17]
- To explore uncertainty, we conducted probabilistic sensitivity analysis **(PSA) with 5000 iterations**.

Tab. 1: Cost-effectiveness of adolescent MenACWY and MenC vaccination scenarios in Germany

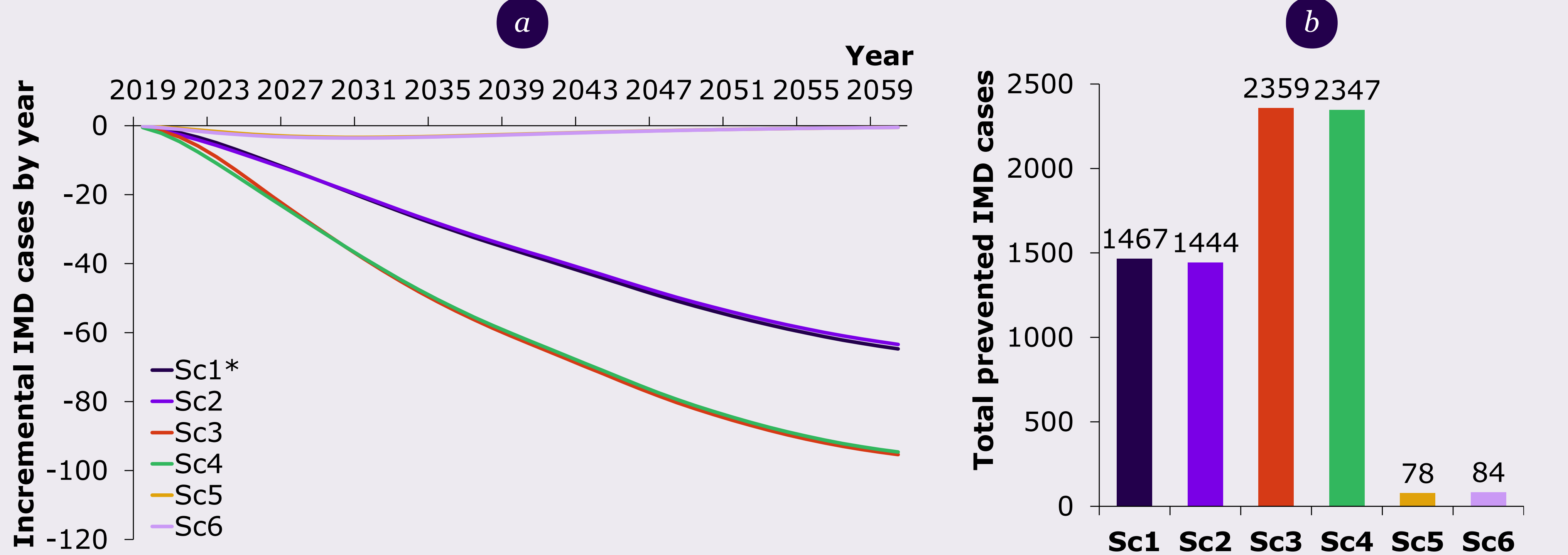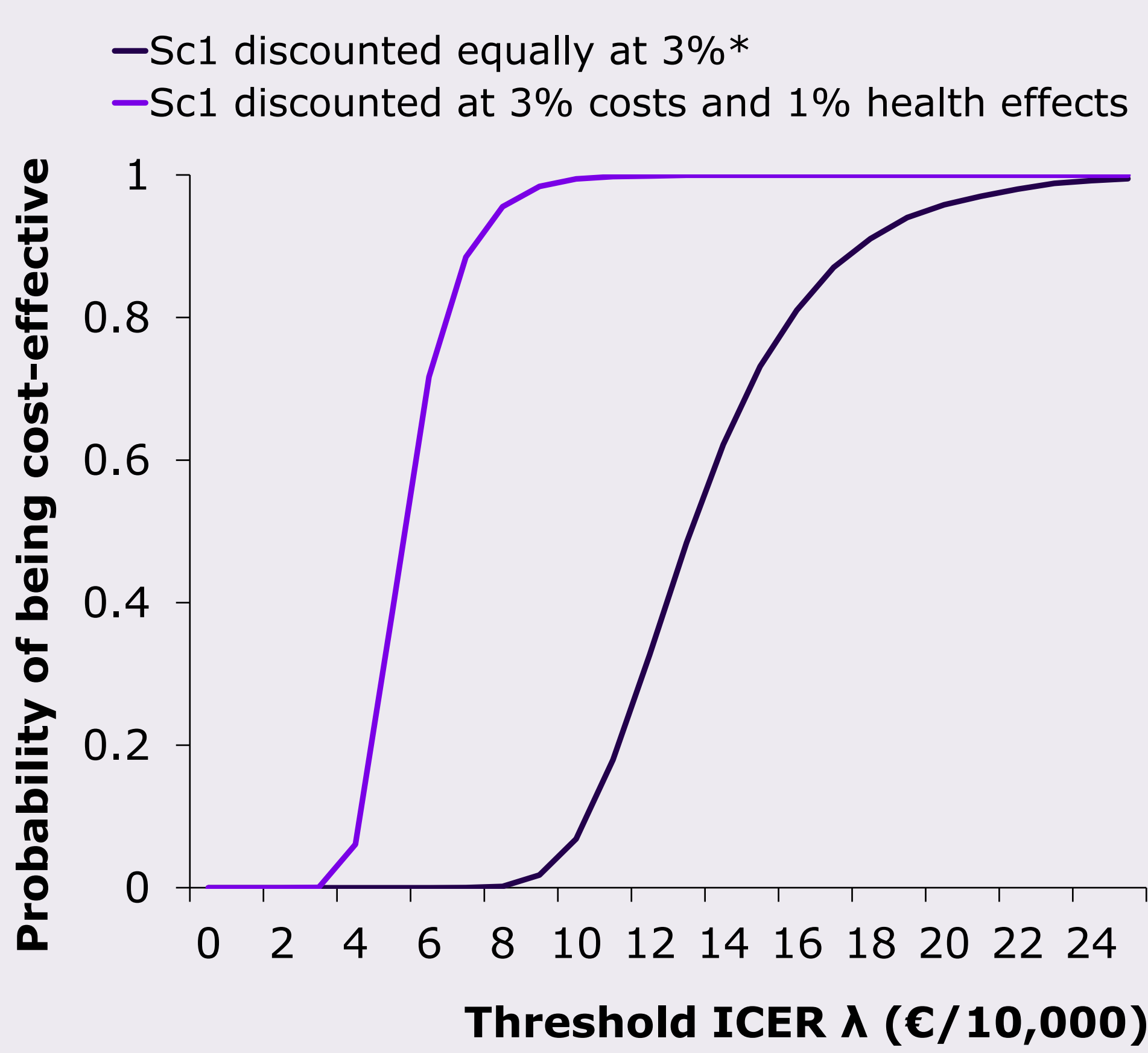| Scenario	Incremental costs (m€)	Incremental QALYs	ICER (€/QALY)
Equal discounting for costs and effects at 3%			
Sc1*	305.9	2333	131,150
Sc2	302.1	2310	130,767
Sc3	291.3	3798	76,701
Sc4	287.2	3803	75,523
Sc5	311.8	255	1,224,305
Sc6	307.7	276	1,113,949
Differential discounting: 3% for costs, 1% for health effects			
Sc1	305.9	5779	52,937
Sc2	302.1	5699	53,013
Sc3	291.3	9239	31,530
Sc4	287.2	9216	31,168
Sc5	311.8	552	565,267
Sc6	307.7	593	519,224

*base case analysis; ICER: incremental cost-effectiveness ratio

RESULTS

- The dynamic transmission model's **predictions match well with observed** cases in Germany. Under the **current vaccination strategy**, the model predicts a further **decrease of MenB and MenC**, opposed to an **increase** of IMD associated with **MenW and MenAY** (see Fig. 1).
- The model estimated the introduction of **MenACWY** adolescent vaccination **in 12–14-year-olds** with an assumed **VEc of 36%** (Sc1) to significantly lower IMD incidence, **preventing up to 64 IMD cases per year** (see Fig. 2a), and **1467 cases** overall **until 2060** (see Fig. 2b).
- The majority of prevented cases was due to **herd effects**, decreasing IMD incidence across all age groups.

- The CUA resulted in incremental cost-effectiveness ratios (ICERs) from **€75,523 to €131,150 per QALY** for scenarios with **MenACWY in adolescents** with equal discounting (Sc1-Sc4, see Tab. 1).
- ICERs under **differential discount rates** were considerably lower, ranging between **€31,168 and €53,013 per QALY** (Sc1-Sc4, see Tab. 1).
- The introduction of MenC in adolescents resulted in ICERs of **€1,113,949 and €1,224,305 per QALY** (Sc5-Sc6) at equal discount rates.
- The **application of a QAF** lowered the ICERs to **€35,399 to €61,207 per QALY**, with an **ICER of €61,167 in Sc1** under equal discount rates.
- Fig. 3 displays the cost-effectiveness acceptability curve (CEAC) from the PSA.

Conclusions

Our findings indicate that the introduction of MenACWY vaccination in adolescents in Germany could substantially lower IMD cases across all age groups. In contrast, adolescent MenC vaccination has minor impact. Given the significant health care resource use associated with IMD, the results suggest economic benefits of implementing a MenACWY booster vaccination.

Fig. 3: Cost-effectiveness acceptability curve (CEAC) for Sc1 discounted equally and differentially

*base case analysis; ICER: incremental cost-effectiveness ratio

References
[1] Christensen et al. Lancet Infect Dis. 2010;10:853. [2] Read et al. Lancet. 2014;384:2123. [3] Carr et al. Clin Microbiol Infect. 2022;28:1649. [4] Maiden et al. J Infect Dis. 2008;197:737. [5] Rieck et al. Epid Bull. 2019;18:14. [6] Campbell et al. Clin. Vaccine Immunol. 2010;17:840. [7] Campbell et al. *Lancet Child Adolesc Health*. 2022;6:96. [8] Trotter et al. *Lancet*. 2004;364;365. [9] Christensen et al. *Vaccine*. 2013;31:2638. [10] CompuGroup Medical. portal.cgmlauer.cgm.com/LF (accessed Aug. 2023). [11] Scholz et al. *Infect Dis Ther*. 2021;11:1311 [12] Scholz et al. *Vaccine*. 2019;37:1692. [13] Shen et al. *BMC Public Health*. 2022;22:1078. [14] Christensen et al. *BMJ*. 2014;349:g5725. [15] JCVI. Minute of the meeting on Tuesday 11 and Wednesday 12 February 2014. [16] Christensen et al. *Vaccine*. 2017;35:208. [17] Neri et al. *Value Health*. 2023;26:1535.