Original Article

Twins with at least one with CHD and their immunisation status in direct comparison—are both twins complying with the German immunisation recommendations?

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Background: Patients with congenital heart defects (CHDs) are at higher risk for infectious diseases. This may partly be due to frequent hospital stays and the associated exposure to pathogens. This study aims to provide a comprehensive overview of immunisation coverage among twins in which at least one twin has CHD. Confounding factors from shared environments and genetic components can be controlled through co-twin control analysis, thus minimising confounding effects.

Methods: In the framework of the cross-sectional twin study "Same Same, but different?" twins, with at least one of them having CHD aged 3 to 99 years, were recruited nationwide in Germany between August 2019 and December 2022. Their primary immunisation status based on the German Standing Committee on Vaccination (STIKO) and immunisation against respiratory diseases, including influenza, respiratory syncytial virus (RSV), pneumococci, and coronavirus disease 2019 (COVID-19), were assessed and compared between the twins.

Results: In total, 64 twins (128 individuals) were included for direct twin comparison. Overall, 56.3% of the twins reached complete primary immunisation status, negatively influenced by hospitalisation duration [odds ratio (OR): 0.98; 95% confidence interval (CI): 0.96–0.99; P=0.01]. Compared to their healthy twin, twins with CHD received their rotavirus vaccine significantly later (P=0.04). Only 3.1% of the twins with CHD received the pneumococcal vaccine recommended for high-risk patients. A higher number of catheter interventions can lead to a higher number of patients receiving the pneumococcal vaccine (OR: 1.79; 95% CI: 1.16–2.76; P=0.009). The direct twin comparison showed a significant difference between the twins in vaccination against influenza (P=0.007), although it is recommended for CHD patients and their household contacts—including their twin. A higher number of surgeries (OR: 1.51; 95% CI: 1.12–2.05; P=0.007) and catheter interventions (OR: 1.49; 95% CI: 1.00–2.21; P=0.049) increase the probability of influenza vaccination in CHD patients.

Conclusions: In the direct twin comparison, twins are similarly vaccinated except for RSV and influenza. Immunisation against influenza in twins should be improved. With new upcoming RSV vaccines, existing

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recommendations must be reconsidered and adapted. Another disturbing fact is that only 30% of infants are vaccinated against pertussis and pneumococcus within the primary recommended timeframe, even though they are exposed at high risk during infancy. Further education of parents, patients, and medical staff might lead to higher vaccination coverage, especially in pneumococcal vaccines recommended for high-risk patients. We must provide sufficient information on the importance of vaccinations and their side effects for parents' and patients' decision-making.

Keywords: Twins study; congenital heart defects (CHD); immunisation; vaccination; 'Same Same but different'

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Introduction

With the first successful vaccine developed by Edward Jenner in the late 18th century, an era of vaccination for infection prevention started (1). It has been one of the most effective public health interventions, protecting millions of people from infectious diseases (2). Patients with chronic diseases such as congenital heart defects (CHDs) are particularly vulnerable to infectious diseases like respiratory infections caused by, e.g., influenza (3,4). With around 1% of live births affected by CHD (5), vaccination is an essential component of their overall care (6). Various studies have evaluated the effectiveness of different vaccines, such as influenza and pneumococcal vaccines, in this population (7,8).

In Germany, immunisation recommendations have been present since the 19th century; the German Standing Committee on Vaccination (STIKO) was founded in 1972 (9), introducing systematic vaccination recommendations nationwide (10). The recommendations have been updated yearly ever since and led to the decline of vaccine-preventable infections (11).

Highlight box

Key findings
- Twins are similarly vaccinated regarding primary immunisation.
- There is a need for improvement in immunisation against pneumococci, influenza, and respiratory syncytial virus (RSV).

What is known, and what is new?
- Sufficient immunisation coverage is known as a crucial component to prevent several diseases. Especially children dealing with chronic diseases such as congenital heart defects (CHD) are at higher risk.
- Primary immunisation coverage is lower in children with CHD than in comparable healthy children, even though there are existing immunisation recommendations.
- The results on the immunisation status of people with and without CHD were obtained through a unique analysis of twin pairs with at least one CHD twin. This makes it possible for the first time to largely control for potential influencing factors such as socioeconomic status, parental education level, and genetic disposition.

What is the implication, and what should change now?
- With new upcoming RSVmab and vaccines, existing recommendations must be reconsidered and adapted.
- Vaccination with the 23-valent pneumococcal polysaccharide vaccine is low and should be improved.

Rationale and knowledge gap

However, vaccination coverage among children with CHD is lower than that of healthy school-age children (12). By now, there is no clear explanation for that, especially since explicit recommendations for children with CHD and their households are available. A lower socioeconomic status may be associated with less or misinformation on the vaccination recommendations, and lower educational levels may be responsible for lower vaccination rates. To try to exclude these potentially influencing factors, we analysed data on vaccination coverage in twins with at least one with CHD.

This analysis aims to provide a comprehensive overview of vaccination coverage among twins with at least one CHD. Confounding factors from shared environments and genetic components can be controlled through co-twin control analysis, thus minimising confounding effects.

Primary immunisation recommended for every child by STIKO will be evaluated (10). In addition, this study will primarily focus on the vaccinations specifically recommended for CHD patients (13,14) and their household contacts, in this context, their twins (10). During the current post-coronavirus disease 2019 (post-COVID-19) situation, respiratory infections caused by other pathogens

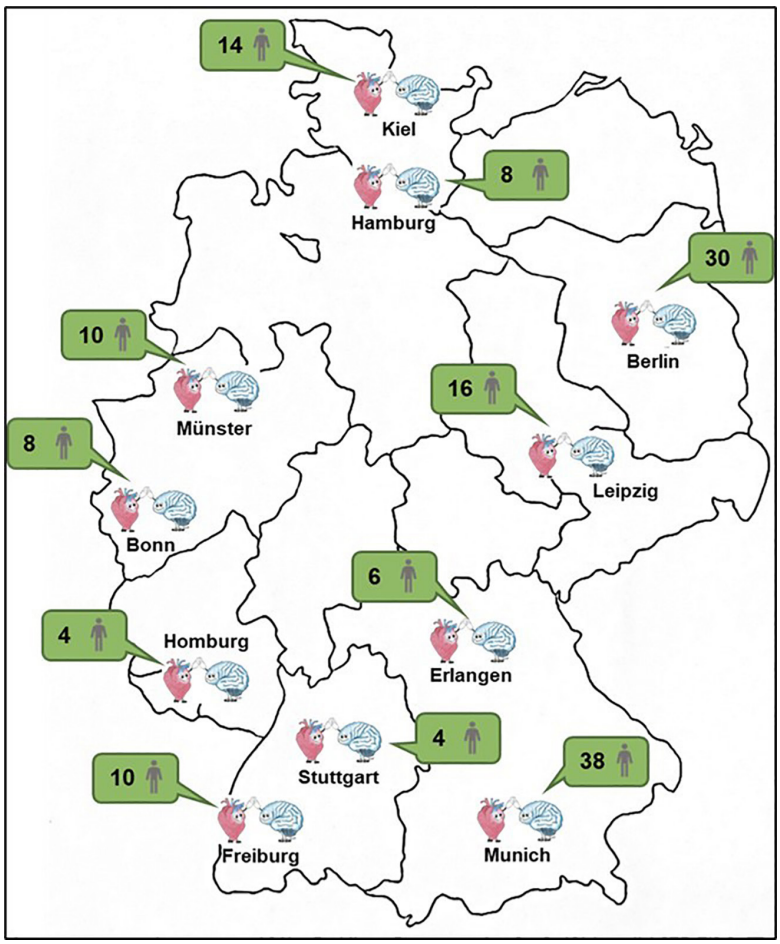

Figure 1 Overview of the examination locations and number of included twins by federal state. N, number of patients recruited for this study.

are rising (15-17). The extent to which families with CHD patients adhere to the corresponding recommendations will be evaluated in the first study of twins with CHD in Germany. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-24-302/rc).

Methods

Study population

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). In the framework of the cross-sectional twin study "Same Same, but different?" [Approved by the Medical Ethics Committee Charité Mitte on 26 June 2018 (EA2/086/18)], 74 twin pairs registered in the National Register for Congenital Heart Defects (NRCHD) were recruited nationwide between August 2019 and December 2022 (*Figure 1*). Inclusion criteria were twins aged between 3 and 99 years old, with at least one of the twin siblings having CHD (18). Patients were excluded if they had surgery or catheter intervention within the last 6 months, massive mental retardation not allowing testing, other medical examinations on the test day, or insufficient language skills (18). Informed consent was taken from all individual participants and parents. After excluding seven twin pairs without vaccination information, 67 pairs remained for further statistical analysis and 64 for the direct twin comparison (*Figure 2*).

The twins or their guardians were asked to bring the vaccination cards. Primarily, we focused on the routine immunisation schedule by the STIKO which includes the following vaccinations: rotavirus, tetanus, diphtheria, pertussis, haemophilus influenzae type B, poliomyelitis,

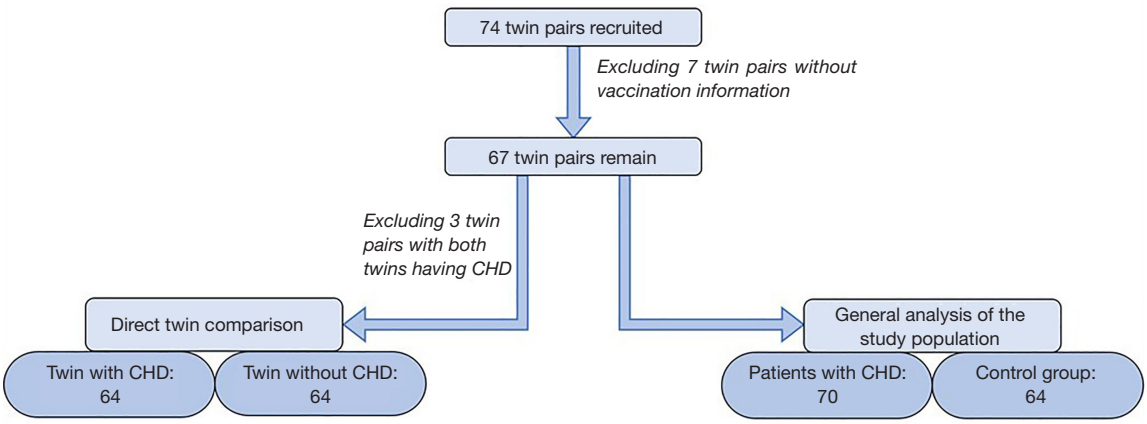

Figure 2 Flow chart of the study population. CHD, congenital heart defect.

hepatitis b, pneumococci (13-valent), meningococci C, Measles/Mumps/Rubella, varicella, human papillomavirus (HPV), and influenza (10) (*Figure 3*). Vaccinations against Measles, Mumps, and Rubella (MMR) are generally applied as a combination vaccine; hence, they are treated as one vaccination (MMR). Complete primary immunisation was achieved if patients were immunised according to the routine immunisation schedule (10) (*Figure 3*). Immunisation against Herpes zoster, recommended for individuals 60 years and above, was excluded due to the relatively young age of our study population.

There are also vaccinations specifically recommended for CHD patients, like the pneumococcal vaccine for high-risk patients (10), vaccination against influenza (10), and respiratory syncytial virus (RSV) immunoprophylaxis (14). Vaccination against influenza is recommended for CHD patients and their household contacts like family members, caretakers, etc. Due to the topicality, we have also evaluated vaccination against coronavirus (COVID-19).

We used the STIKO recommendations for all vaccinations except the RSV immunoprophylaxis to analyse the immunisation data. For RSV immunoprophylaxis, the Association of the Scientific Medical Societies in Germany (AWMF) recommendations were applied (14).

Patients who did not receive vaccination due to its later release/recommendation date were excluded but were included in the final analysis of the complete primary immunisation status (*Table 1*). Additionally, demographic variables (e.g., age, gender) and medical variables (e.g., diagnosis, number of surgeries, interventions, hospitalisation duration) were assessed. The severity of CHD was classified according to the ACC classification by Warnes *et al.* (19).

STIKO

The STIKO is an independent advisory group of 12 to 18 unpaid members the German Federal Ministry of Health appoints. They develop national recommendations for the use of licensed vaccines in Germany. Although the recommendations are not legally binding, they form the basis for the federal states' vaccination guidance and the Federal Joint Committee's vaccination directive (20). Since March 2020, vaccination against Measles has been the only mandatory vaccination in Germany (21).

AWMF

Consisting of 182 scientific medical societies and three associated societies, the AWMF has dealt with interdisciplinary medical issues since 1962 (22). The AWMF also provides interdisciplinary guidelines, e.g., the guideline on immunisation against RSV published by the German Society for Pediatric Infectiology and seven other medical societies, including the German Society for Pediatric Cardiology (14).

Statistical analysis

Descriptive statistics were used for categorical variables, and numerical variables were presented through means and standard deviations. χ^2 or Fisher's exact test was used for comparing dichotomous variables for general comparison. The paired Student's *t*-test and McNemar test were applied for twin comparisons. A binary logistic regression model was used to determine CHD treatment's influence on CHD patients' vaccination behaviour whereby odds

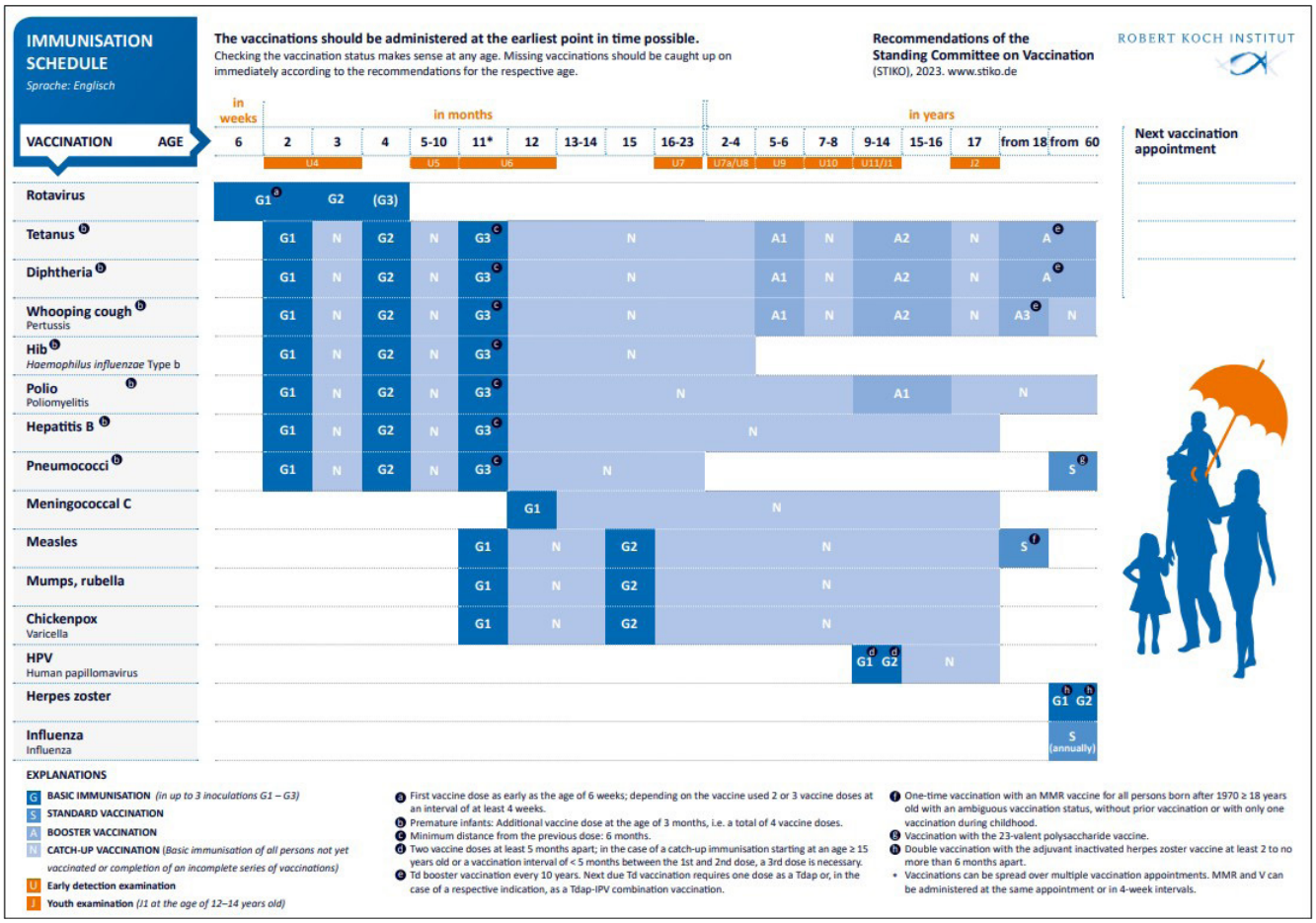

Figure 3 Official routine immunisation schedule by the Standing Committee on Vaccination (10).

ratio (OR) and confidence interval (CI) means. SPSS V.29 (SPSS Inc., Chicago, Illinois, USA) and RStudio 2022.07.1 (Posit Software, Boston, Massachusetts, USA) were used for statistical analyses. With a two-sided P value <0.05, the statistical significance was determined.

Results

In total, 67 twins were included with complete immunisation information (*Figure 1*). Out of the 67 twins 64 were discordant for CHD and used for twin analysis. Regarding the gender distribution, the twins were as follows: 19 male pairs, 33 female pairs, and 15 opposite-sex twins.

Overall, the most frequent CHD diagnoses among CHD patients were univentricular heart (UVH) circulation at 27.1%, tetralogy of Fallot (TOF) at 18.6%, and coarctation of the aorta (CoA) at 10.0%. Out of the 70 CHD patients, 7 (10%) have simple CHD, 28 (40%) moderate CHD, and 35 (50%) complex CHD. Further information on the general study population is shown in *Table 2*.

Primary immunisation recommended for all individuals by the STIKO

Of the 64 healthy twins, 38 (59%) were primarily vaccinated according to the STIKO routine immunisation schedule, while 37 (58%) twins with CHD received all recommended primary vaccinations. 56.3% of the 64 twin siblings have completed primary immunisation. Out of the male twins, 60.4% got complete primary immunisation status, and 57.3% of the female twins were completely immunised, according to STIKO recommendations. The primary immunisation rates were above 90%, except for rotavirus, at 61.3%, and HPV, at 47.6%, in CHD twins. In comparison, 64.5% of the healthy twins were vaccinated against rotavirus and 52.4% against HPV (*Figure 4*).

Table 1 Overview of subsequently recommended immunisations and number of patients included for analysis

Immunisation	Recommended since	No. of twins included for analysis
Coronavirus disease 2019	November 17th, 2022 for children aged 6 months to 4 years	0
	December 17th, 2021 for children aged 5 to 11 years	10
	June 10th, 2021 for children aged 12 to 17 years	14
	December 27th, 2020 for adults	14
Rotavirus	2013	62
Human papillomavirus	2018 for boys at 9 years	18
	2007 for girls at 9 years	32
Meningococci C	2006	122
Pneumococci (13-valent)	2006	116
Varicella	2004	118
Respiratory syncytial virus	2003 for infants (with an underlying disease/condition according to the AWMF recommendations) younger than 2 years	118
Complete primary immunisation		134

AWMF, Association of the Scientific Medical Societies in Germany.

Table 2 General information on the study population

Variables	Patients with CHD	Twin without CHD	Twin with CHD for direct twin comparison
Number of patients	70 (52.2)	64 (47.8)	64 (50.0)
Age (years)	12.26±7.62 (3/38)	11.15±6.96 (3/38)	11.15±6.96 (3/38)
Sex (female)	45 (64.3)	37 (57.8)	39 (60.9)
Most frequent diagnosis			
UVH	19 (27.1)	–	17 (26.6)
TOF	13 (18.6)	–	11 (17.2)
CoA	7 (10.0)	–	7 (10.9)
No. of surgeries	2.5±2.6 (0/10)	0	2.6±2.6 (0/10)
No. of catheter interventions	1.3±1.8 (0/9)	0	1.3±1.7 (0/9)
Hospital stay (days)	43.6±46.9 (3/185)	0	44.4±47.1 (3/185)

Data are presented as mean ± standard deviation (minimum/maximum) or number (percentage). CHD, congenital heart defect; UVH, univentricular heart; TOF, tetralogy of Fallot; CoA, coarctation of the aorta.

Rotavirus vaccination was administered later than recommended in 41.9% of the twins with CHD, while only 19.4% were vaccinated on time. In 29% of the twins without CHD, rotavirus vaccination was delayed, while 35.5% of them were vaccinated on time. There was a significant difference between the twins regarding the delay of rotavirus vaccination (P=0.040). The twins with CHD with delayed or no rotavirus vaccination were first hospitalised at a mean age of 0.57±1.93 years.

Out of the nine male twins with CHD included for analysis of HPV immunisation, 2 (22.2%) have received the vaccine, while 61.5% of the female twins with CHD were vaccinated entirely against HPV.

MMR vaccination coverage was exceptionally high; every twin was vaccinated, except for one with CHD, who received a heart transplant.

By comparing the twins, no significant differences in their primary immunisation status could be found (*Figures 4*,*5*).

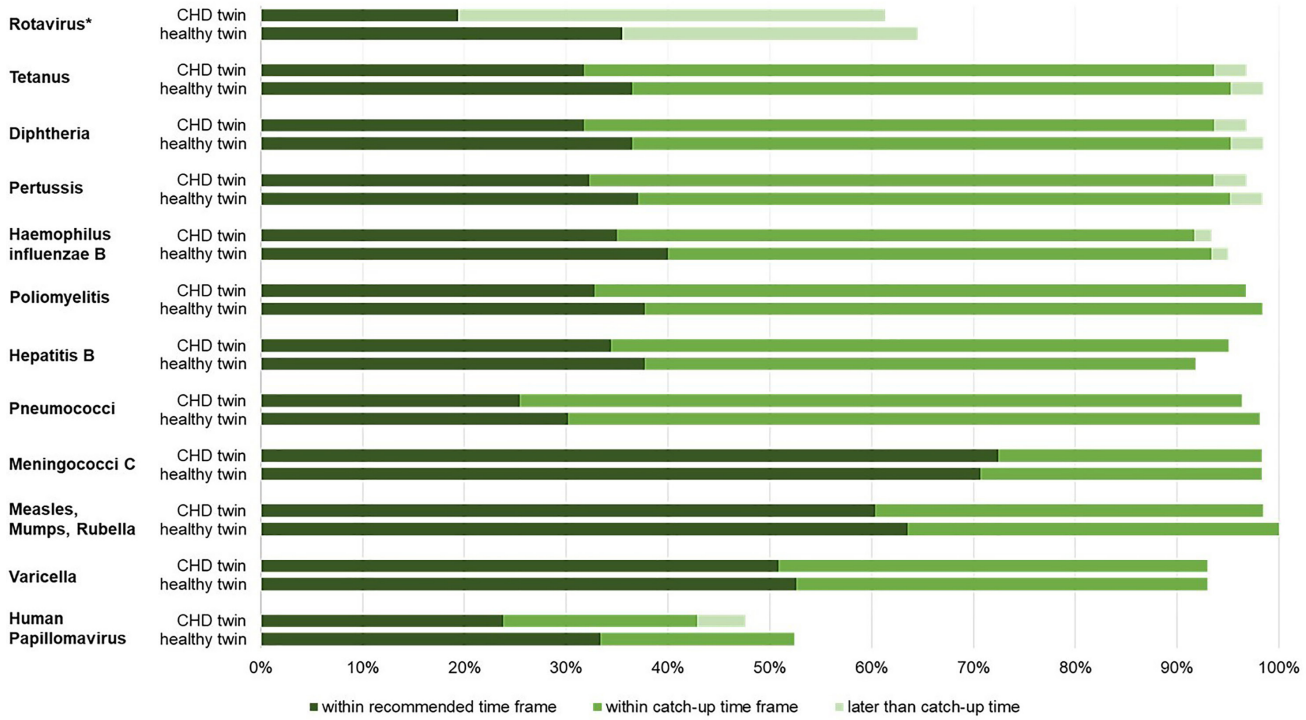

Figure 4 Primary immunisation coverage based on the age-dependent STIKO recommendations (within recommended time frame, within catch-up time frame and later than catch-up time frame). *, there is no catch-up time frame for vaccination against rotavirus. STIKO, Standing Committee on Vaccination; CHD, congenital heart defect.

Immunisations recommended for CHD patients and vaccination against COVID-19

In general, 63.5% of the CHD twins were immunised against influenza and 45.3% against RSV, while only 3.1% received the pneumococcal vaccine for high-risk patients. Significantly more twins with CHD were immunised against influenza (P=0.007) and RSV (P<0.001) compared to their healthy twin siblings (*Figure 5*).

With 77.8% vaccination against COVID-19, it has the highest coverage among CHD patients' recommended immunisations against respiratory infections. Both twins are equally vaccinated against COVID-19.

CHD severity, treatment, and immunisation status

To assess the influence of CHD treatment on the immunisation status, all 70 patients with CHD were analyzed.

Vaccination was delayed in 13 of the 19 (68.7%) CHD patients who received the rotavirus vaccine. Out of these 13 patients, 10 (76.9%) were hospitalized during the recommended time for their rotavirus vaccination. In 4 hospitalized CHD patients, vaccination delay was caused by their frequent or prolonged hospital stay.

While 60.7% of the patients with moderate CHD and 57.1% with complex CHD reached complete primary immunisation status, only 28.6% of the patients with simple CHD received all immunisations recommended by STIKO for all individuals (*Table 3*).

Regarding the immunisations recommended for CHD patients, a significant difference between patients with moderate CHD and patients with complex CHD could be found in vaccination against influenza (P=0.005) and RSV (P=0.009). In both, patients with complex CHD have higher vaccination coverage (*Table 3*).

The influence of CHD treatment, such as surgeries, catheter interventions, and hospital stays, on vaccination behaviour is shown in *Figure 6*. A higher number of surgeries result in more CHD patients getting vaccinated against influenza (OR: 1.51; 95% CI: 1.12–2.05; P=0.007), while higher number of catheter interventions can lead to higher number of patients receiving the influenza vaccine (OR: 1.49; 95% CI: 1.00–2.21; P=0.049) and pneumococcal vaccine for high-risk patients (OR: 1.79; 95% CI: 1.16–2.76;

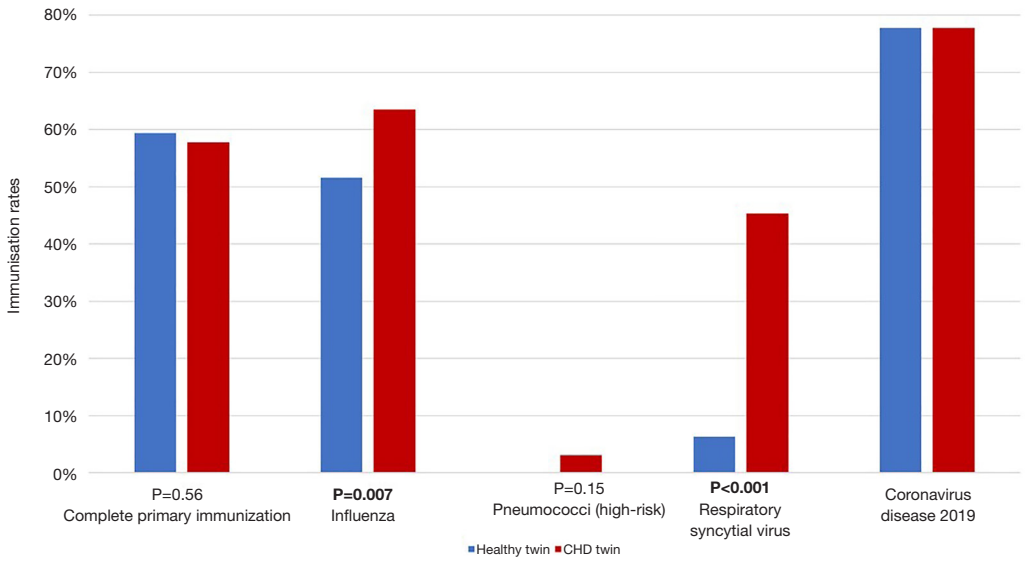

Figure 5 Complete primary immunisation status and coverage of immunisations recommended for CHD patients and other vaccinations. The level of significance using paired *t*-test for twin comparison P<0.05. Pneumococci for high-risk patients and RSV are only recommended in patients with CHD. Significant values are bold. CHD, congenital heart defect; RSV, respiratory syncytial virus.

Table 3 Primary immunisation and vaccination against respiratory infections among CHD severities

Immunisation	Simple, n (%)	Moderate, n (%)	Complex, n (%)	P values		
				Simple *vs.* moderate	Moderate *vs.* complex	Complex *vs.* simple
Complete primary immunisation	2 (28.6)	17 (60.7)	20 (57.1)	0.20*	0.77	0.22*
Pertussis	7 (100.0)	27 (96.4)	34 (97.1)	>0.99*	>0.99	>0.99*
Influenza	3 (42.9)	13 (46.4)	28 (80.0)	>0.99*	**0.005**	0.06*
Pneumococci (23-valent)	0	1 (3.6)	5 (14.3)	>0.99*	0.21*	0.56*
Respiratory syncytial virus	2 (28.6)	8 (32.0)	19 (67.9)	>0.99*	**0.009**	0.09*
Coronavirus disease 2019	2 (50.0)	4 (80.0)	10 (90.9)	0.52*	>0.99	0.15*

*, Fisher's exact test instead of χ^2 was used due to an expected value below. Significant values are bold. CHD, congenital heart defect.

P=0.009). Longer hospitalization duration negatively influences CHD patients' complete primary vaccination status (OR: 0.98; 95% CI: 0.96–0.99; P=0.01).

Discussion

Primary immunisations recommended by the STIKO

There was no significant difference between the twins regarding their primary immunisation coverage. Therefore, CHD did not influence the parents' decision on vaccination to vaccinate the twins differently.

Overall, the HPV and rotavirus immunisation coverage was lower than most of the recommended primary immunisation rates.

In the general German population, 51.1% of the 18-year-old female population were immunised against HPV, while only 1.3% of the 18-year-old male population received the vaccine (23). In comparison, HPV immunisation

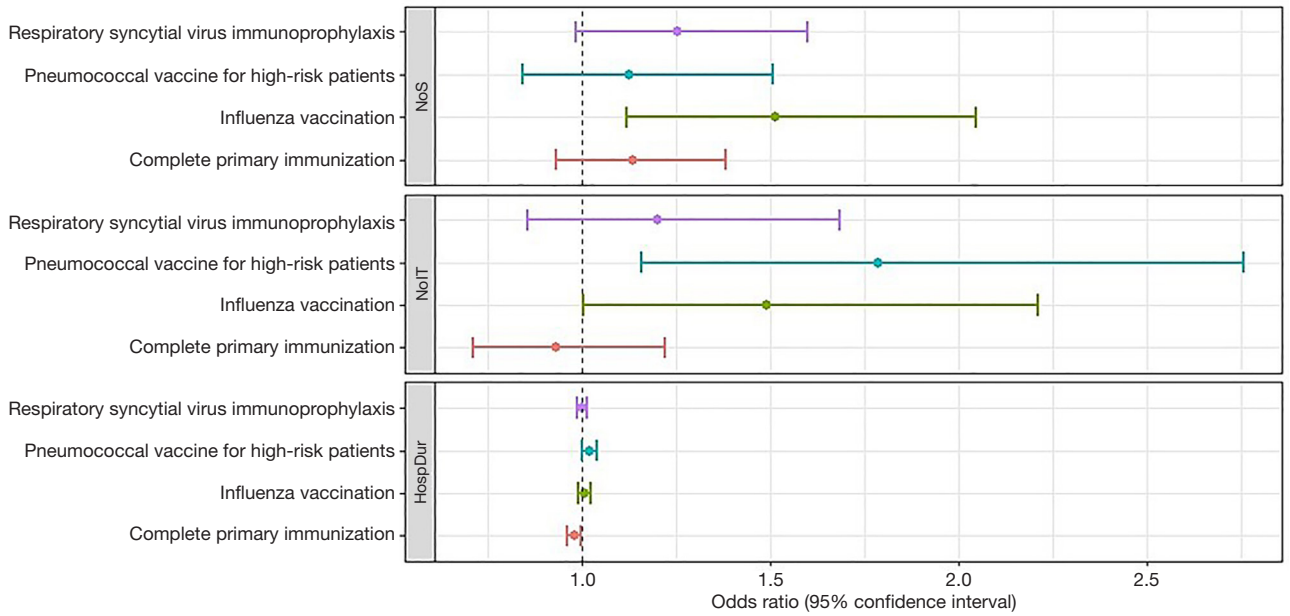

Figure 6 Results of the logistic regression model of primary immunisation and recommended immunisations for CHD patients regarding CHD treatment. CHD, congenital heart defect; NoS, number of surgeries; NoIT, number of catheter interventions; HospDur, hospitalization duration.

coverage in our study population was higher. The HPV coverage difference between the male and female population can be explained by its later introduction for boys in 2018 (24) compared to the pre-existing recommendations for girls 11 years prior (25).

Twins with CHD received their rotavirus vaccination significantly later than their twin siblings without CHD. The twins with CHD with delayed or no rotavirus vaccination were first hospitalised at a mean age of 0.57±1.93 years, around the age of 0.42 years at which the last rotavirus vaccine shot should be administered. The early age of hospitalization and treatment of CHD possibly resulted in the delay or even non-vaccination against rotavirus.

There are other possible explanations for non-vaccination. Due to the relatively late recommendation of the vaccination in 2013 (26), immunisation against rotavirus might not be as integrated into the vaccination routine as other primary vaccinations, leading to a lower coverage rate.

In addition, studies have shown that vaccination against rotavirus can lead to intussusception in 1.7/100,000 infants vaccinated at the recommended age and 5.6/100,000 infants above the recommended age (27-30), resulting in parental concern and thus non-vaccination.

However, CHD patients are hospitalised early and thus are especially at risk for nosocomial infection during hospitalisation (31). They should receive the rotavirus at the recommended age. Studies have shown that the rotavirus vaccine effectively reduced infections and nosocomial diarrhoea, often occurring in hospitalized infants and children (31,32). Against the recommendations only about 30% of infants were vaccinated within the primary recommended timeframe, even though they are at high risk during infancy. Especially since protection from particularly severe diseases is only given until completion of the primary course, delays cause them to be vulnerable for longer and this holds true for all infants. In this regard, discussing how this vital information can be better communicated to parents to protect children is essential.

Fortunately, all twins except one have been vaccinated against MMR, which has been mandatory for attending German kindergarten and school since 2020 (21); therefore, high coverage was expected. The only patient not immunised against MMR has received a heart transplant within the first two life months. Post-transplantation due to the immunosuppression, live vaccines like the MMR vaccine are contraindicated (33).

Vaccinations recommended for CHD patients and immunisation against COVID-19

Overall, CHD patients were at higher risk for severe

respiratory infections caused by, e.g., RSV (3), influenza (4), and pneumococci (34). Therefore, immunisation recommendations have been developed accordingly for high-risk groups, including CHD patients (6,10,14).

Significantly more twins with CHD were immunised against RSV and influenza compared to their twin siblings without CHD.

The significant difference between the twins regarding their RSV immunisation coverage was to be expected. According to the current AWMF recommendations on RSV immunoprophylaxis in Germany, infants at risk, such as CHD patients or prematurely born, should get an RSV immunoprophylaxis (14). It is proven that infants with CHD are at higher risk of respiratory tract infections caused by RSV (35), resulting in hospitalisation (36). RSV immunoprophylaxis can reduce the risk of hospitalisation in infants with hemodynamically relevant CHD (37).

However, due to the increasing number of RSV infections, new RSVmab, such as nirsevimab, and RSV vaccines have been developed and introduced (38-40). Unlike palivizumab, which must be administered monthly during RSV season, nirsevimab only needs to be administered once per RSV season. This could lead to expanding the current recommendations to include family members of infants at risk for severe RSV infection for indirect protection, similar to the current recommendation on immunisation against influenza.

Patients at higher risk for severe infection due to chronic diseases, patients above 60 years, or pregnant women should get an influenza immunisation (10). For indirect protection, it is also recommended for household contacts of the mentioned groups at risk, e.g., family and caretakers (10). Despite the recommendations, immunisation coverage was significantly lower in our healthy twins than their twins with CHD. Due to the higher risk of mortality and morbidity in CHD patients affected by viral pneumonia caused by influenza (7), parents might think that only the CHD twin needs to be immunised against influenza, therefore resulting in the different immunisation coverage between the twin siblings. However, there was evidence that family members like siblings can be a risk factor for hospitalisation due to influenza in infants (41). Therefore, immunisation against influenza in household contacts, which was a protective factor (41), should be improved.

Despite the evidence on the effectiveness of pneumococcal vaccines for high-risk patients (42), also lowering the risk for cardiovascular events (43), immunisation coverage in our twins with CHD is low. In Germany, a pneumococcal vaccine for high-risk patients was recommended in 2016 (13). According to Helm *et al.*, parents were unaware of the recommendations, which resulted in low immunisation coverage in patients with severe CHD (44). In addition, with the 13-valent pneumococcal conjugate vaccine (PCV13) being part of the primary immunisation schedule (10), CHD patients or their parents might think that further vaccination against pneumococci is unnecessary. Regarding the incidence of invasive pneumococcal disease (IPD) in Germany, the number of IPDs caused by PCV13 preventable pneumococcal serotypes decreased since its recommendation in 2006 (15). On the contrary, IPD, which the pneumococcal vaccine for high-risk patients could prevent, increased over the years, even after its recommendation in 2016 (15). Less is known about IPD in adults with CHD (ACHD), but IPD in patients with chronic heart diseases, including valve diseases, are at higher risk of severe infection (34). Therefore, medical staff should raise awareness for the pneumococcal vaccine for high-risk patients in parents and patients with CHD.

Although vaccination against COVID-19 is relatively new, 80% of our study population was vaccinated. According to the German Society for Pediatric Cardiology and Congenital Heart Defects (DGPK), CHD patients were not at higher risk of severe infections (45). However, the immunisation coverage in our twins was still high. With the COVID-19 pandemic being an everyday topic, parents were probably more likely to get their child vaccinated due to fear of severe infection (46). Additionally, the regulations during the COVID-19 pandemic, enabling social life by meeting one of the 3G rules: vaccinated (Geimpft), recovered (Genesen), tested (Getestet), might have encouraged vaccinating willingness (47).

CHD severity, treatment, and immunisation status

Regarding the severity of CHD, significantly more patients with complex CHD received immunisation against RSV and influenza compared to patients with moderate CHD.

According to the AWMF recommendations, patients with hemodynamically relevant CHD must be immunised against RSV. However, the recommendations do not clearly define which CHD are considered hemodynamically relevant. So, it is up to the treating physician to decide whether the patient needs to be immunised, resulting in a significantly higher RSV immunisation coverage among patients with complex CHD.

Nonetheless, RSV immunisation must be improved, especially in patients with moderate CHD.

Regarding the influence of CHD treatment, the higher number of surgeries and catheter interventions increased the possibility of patients getting vaccinated against influenza. A higher number of catheter interventions was associated with higher pneumococcal vaccination for high-risk patients' coverage, indicating that these CHD patients were more aware of the vaccination. At that point, it would be interesting to see who made them aware of the vaccination: medical staff at the hospital, general practitioners, or resident paediatricians.

More extended hospital stays negatively influenced the primary immunisation status in patients with CHD, which is plausible due to the tight routine vaccination schedule, especially in the early months of life (10).

Conclusions

In conclusion, twins with and without CHD were similarly vaccinated except for RSV and influenza. In particular, vaccination against influenza in twins of CHD children and adolescents should be improved for better prevention by following the recommendations. The existing recommendations must be reconsidered and adapted to new upcoming RSV vaccines. Another disturbing fact is that only 30% of infants are vaccinated against pertussis and pneumococcus within the primary recommended timeframe, even though they are exposed at high risk during infancy. As the COVID-19 pandemic proved, constant education of parents, patients, and medical staff can lead to higher immunisation coverage, which must be significantly improved in pneumococcal vaccine for high-risk patients. Further investigation is needed to understand the reasons behind the decisions for and against certain vaccinations for better education of parents and patients. Sufficient information on vaccinations' importance and side effects must be provided for parents' and patients' decision-making.

Limitations

It could be argued that predominantly informed families register their children in the NRCHD and that there might also be a compliance bias here. Nevertheless, they do not meet the vaccination recommendation for households/siblings with a CHD child, especially in terms of respiratory infections. While the study yielded generally good immunisation results, there is a limitation in our ability to identify the causes of non-vaccination. This should be included in future studies to explore and identify positive and negative factors influencing the willingness to vaccinate.

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Footnote

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