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How baby's first shot determines the development of maternal attitudes towards vaccination

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ABSTRACT

Background: The attitude towards vaccination is a major determinant of vaccination behavior; this also includes parents' attitudes towards the immunization of their child. Negative attitudes have been associated with vaccine hesitancy and outbreaks of infectious diseases throughout the globe. This study aimed to assess how and why attitudes become more pro-vaccine or vaccine-skeptical over time, and which sources are especially influential in this process.

Methods: Prospective cohort study with measurements at time of recruitment during pregnancy and at +3, +6 and +14 months after childbirth with cross-sectional control groups. In total, 351 women entered the longitudinal analyses, while 204, 215 and 173 women were recruited in the cross-sectional control groups, respectively. Inclusion criteria were: (i) being at least 18 years of age, (ii) pregnant, (iii) primigravida, and (iv) living in Germany.

Results: During pregnancy mothers reported rather positive prior experiences with vaccinations. However, their judgment turned significantly more negative after the first vaccination experience with their child. Mixed-effects models showed that these changes were significantly related to increased risk perceptions and concerns about vaccination, which then had a negative impact on the vaccination attitude. In contrast, gaining more vaccine-related knowledge over time positively influenced attitude formation.

Conclusions: During the first year of their child's life maternal attitudes towards vaccination are formed and guide future decisions whether to vaccinate or not vaccinate a child. Strategies should be implemented that improve mothers' experiences when their newborn is vaccinated to prevent the development of vaccine hesitancy.

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1. Introduction

While vaccination is considered to be one of the major medical achievements with great public health impact, a concerning number of parents are vaccine hesitant globally [1]. It is estimated that less than 5–10% of individuals have strong anti-vaccination convictions, but a more significant proportion could be categorized as being vaccine hesitant [1].

Vaccine hesitancy has been defined as a "delay in acceptance or refusal of vaccination despite availability of vaccination services" [2]. A number of models have been proposed that describe vaccine hesitancy on varying levels of resolution [3]. On the meso-level, individual and social influences, contextual influences, as well as vaccine- and vaccination-specific issues play a role [2]. The macro-level model describes vaccine hesitancy as a function of complacency, inconvenience of vaccine delivery, a lack of confidence in vaccines and the system that delivers them [2], and too much calculation in the process of information searching [4]. On the micro-level, the Theory of Planned Behavior (TPB) describes vaccination behavior as a function of the behavioral intention to get vaccinated [5]. The intention results from the attitude towards the behavior, perceived behavioral control, and the subjective norm. Previous research has shown that the attitude towards vaccination is a major predictor of vaccination behavior [3,6]. Additionally, attitude is central to all models of vaccine hesitancy listed above: attitude counts as an individual influence in the meso-level approach, and it is a basic factor in explaining confidence in vaccination in the macro-level model and a primary determinant in the micro-level model of vaccine hesitancy [4]. Scales that measure vaccine hesitancy often assess attitudes towards vaccination (such as the Parent Attitudes About Childhood Vaccine Scale [7]) and have

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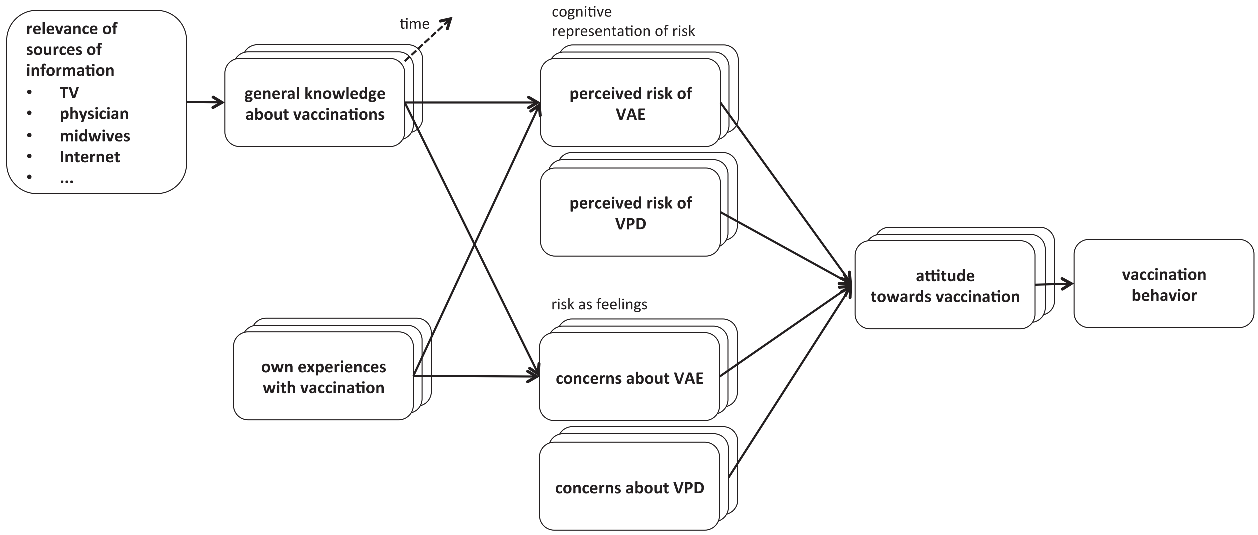

Fig. 1. Conceptual model: The development of the attitude towards vaccination is a function of behavioral beliefs, measured as vaccine-related knowledge and risk perceptions. *Note*: VAE = vaccine-adverse events, VPD = vaccine-preventable disease.

demonstrated the importance of attitudes in vaccine decision making.

Recognizing the importance of attitudes, the American Academy of Arts & Sciences recommended in their research agenda on "Public Trust in Vaccines" that longitudinal studies should be conducted to assess when and how attitudes and beliefs about immunization are formed, how parents learn about vaccines, and how they are influenced by messages from expert and non-expert sources [8]. We implemented a study to address these research questions; in particular, we were interested to investigate the formation of maternal attitudes towards vaccination over time and to identify relevant determinants of the observed changes. Psychologically, the attitude towards certain behavior (eg, vaccination) is determined by behavioral beliefs of whether performing the behavior is related to positive or negative outcomes, and how likely these outcomes are to occur. This can include concerns and affective aspects [9]. Therefore, in this study we used general knowledge about vaccination as well as risk perceptions as behavioral beliefs to predict changes in the attitude towards vaccination over time. Additionally, psychological work has demonstrated the importance of experience-based knowledge in judging risks [10]. Therefore, this work assessed the importance of participants' own vaccination-related experiences as conceptualized in Fig. 1.

2. Methods

2.1. Study design

We conducted a nationwide web-based prospective cohort study with initially pregnant women who gave birth over the study period. Data were collected at recruitment during pregnancy, with three follow-up interviews after giving birth until the child turned 14 months. Participants in this longitudinal cohort comprised the main sample in all analyses (see Fig. 2). To identify possible knowledge distortion effects through repeated participation, cross-sectional control groups were set up for each of the three interviews after giving birth. At recruitment, participants filled in the initial online-questionnaire. Subsequently the EFS Survey software randomly assigned each participant to either the longitudinal cohort or to one of the three cross-sectional control cohorts. In addition to the recruitment interview, those belonging to the longitudinal group were surveyed at +3, +6, and +14 months after childbirth, whereas women of the control groups were surveyed only one additional time (either +3, +6, or +14 months after childbirth). Ethical approval was obtained from the Ethics Committee of the Charité, University Medicine Berlin (EA1/010/12).

2.2. Setting

The study was carried out at population level, recruiting women who were living in Germany. In Germany, an independent national immunization technical advisory group recommends vaccinations, which are then free of charge. Usually general practitioners provide vaccinations for adults and the pediatrician for children. There are no mandates; all vaccinations are voluntary. The timing of the follow-up interviews was harmonized according to the national vaccination schedule at the time of the study. At the age of 3 months, the first two vaccine doses of the hexavalent (tetanus, diphtheria, pertussis, Haemophilus influenzae type b, poliomyelitis, hepatitis B) and pneumococcal vaccine should have been given; at the age of 6 months another dose of these two vaccines; and at age 14 months a booster-dose of hexavalent and pneumococcal vaccines, as well as meningococcal C vaccine and the first measles, mumps, rubella (MMR) and varicella vaccine doses should have been administered (total of 11 vaccine doses, if MMR and varicella are given as separate doses) [11]. Data collection took place between February 2012 and August 2014 with recruitment interviews being performed between February and August 2012.

2.3. Recruitment of participants and incentives

The number of required study participants was determined by a power calculation with the goal to detect possible differences in influenza vaccination coverage among pregnant women as described elsewhere [12]. Accordingly, 300 women were planned for the longitudinal group, 200 for each cross-sectional group. We considered a possible drop-out of approximately 30% leading to 1200 pregnant women to be recruited. Recruitment took place via different health and lifestyle websites targeting pregnant women and parents.[1] Inclusion criteria for both study groups were:

[1] Among others: www.eltern.de, www.sparbaby.de, www.baby-care.de, www.babyclub.de, www.netmoms.de, www.babyforum.de, www.gofeminin.de, www.9-monate.de, www.kidsgo.de, www.impfbrief.de, www.frauenaerzte-im-netz.de., the German Association of Lactation Consultants, German Society of Pediatrics and Adolescent Medicine, the Federal Centre for Health Education.

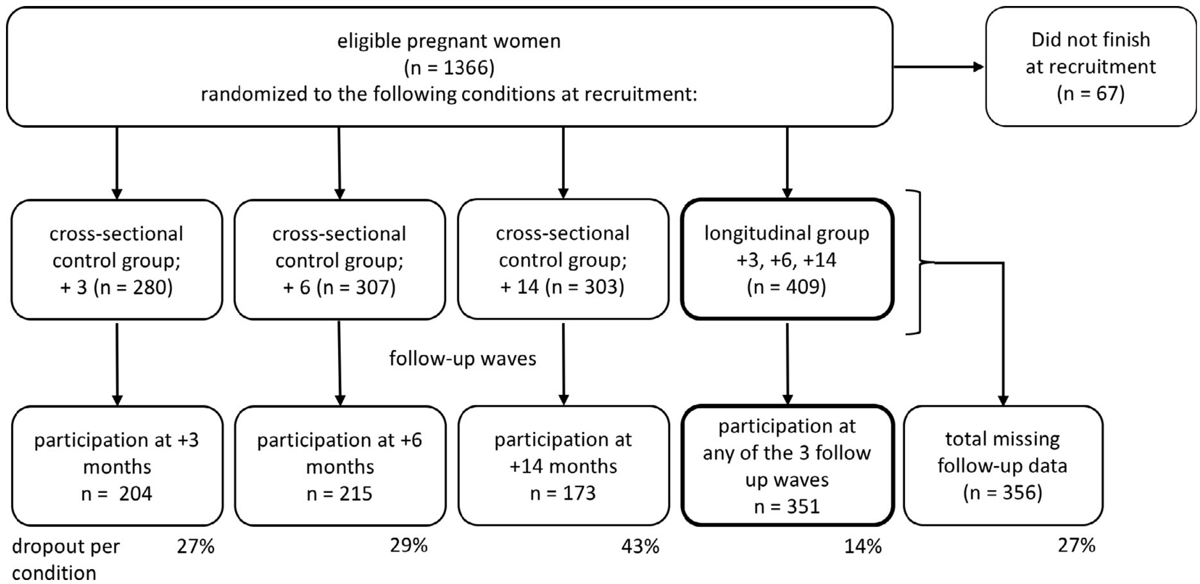

Fig. 2. Study arms and sample sizes over time (+3 months, +6 months, +14 months).

(i) being at least 18 years of age, (ii) pregnant, (iii) primigravida, and (iv) living in Germany. To reduce the possibility of repeated participation, personal codes as well as email addresses were manually cross-checked for duplicates. As an incentive for study participation, women were enrolled in an online lottery draw for vouchers in the cross sectional groups or received vouchers for participating in the longitudinal group. Women were reminded up to 2 times via email to participate in the study.

2.4. Questionnaire

We used structured online questionnaires. Detailed information about all variables and measurement of the constructs are provided in the Supplement, and the questionnaires are available in German language via the online platform "Open Science Framework" [13]. All answers were self-reports. At recruitment, participants were first informed about the study goals and about the tasks and incentives, including the request to participate in one or more future interviews. They were informed about data protection policies and the study's funding sources. After providing informed consent participants were registered for the study by providing their email address.

At recruitment, the pregnant women first filled in the expected date of birth of their child, whether it was their first child (otherwise women were excluded) and in which federal state they lived. The following variables were then collected in the given order and are described in detail in the Supplement: perceived risk of vaccine-preventable diseases (VPDs), perceived risk of vaccine-adverse events (VAEs), concerns about VPDs, concerns about VAEs, general attitude towards vaccination, mother's previous experience with her own vaccinations, immunization-related knowledge, and socio-economic status. During follow-up interviews, we assessed: child's vaccination status, mother's experience with the child's vaccination, importance and frequency of use of different sources of information about vaccination, perceived risk of and concerns about VPDs, perceived risk of and concerns about VAEs, general attitude towards vaccination, immunization-related knowledge.

2.5. Data analysis

Logistic regressions were used to assess whether there was systematic drop-out between follow-up interviews. Repeated measurement ANOVAs were used to assess changes in outcome variables between two interviews and to check for potential differences in attitude towards vaccination between women who dropped out and who remained in the study. Mixed-effects models predicted the change in attitude over time by regressing it on changes in risk perceptions and other predictors. These analyses were conducted with and without imputed data (S1 Table gives an overview of the proportion of missing data per variable; S Methods describes the methods used for imputation). All mixed-effects models were controlled for socio-demographic variables in the second step. Employment, education, age, income, place of residence and country of birth were included as demographic variables. These were relevant predictors of vaccine uptake for pregnant women in previous work [3] and the selection corresponds to previous analyses assessing influenza vaccination behavior based on the same data set [12]. For the mixed-effects models the scales of the predictors were unified using the *percent of maximum possible* score (POMP; see [14]; see Supplement). Linear regression was used to assess the effect of the predictors on the completeness of the child's vaccination status. The selection of predictors for the respective model followed the conceptual model displayed in Fig. 1. All analyses were conducted with SPSS V.23. A p value of <0.05 was considered statistically significant.

3. Results

3.1. Participants

In total, 1299 pregnant women completed the recruitment questionnaire. Of these, 356 did not participate in any additional interviews and were therefore excluded. Of the 943 women included, 351 entered the longitudinal analyses, while 204, 215 and 173 women were recruited to the cross-sectional control groups, respectively. Characteristics of the women in the longitudinal group are displayed in Table 1. Women in the control groups do not differ regarding these characteristics.

3.2. Time

The time from recruitment until the child's birthday was calculated in days. Therefore, in all analyses reported below, time is measured in days ranging from –X (individual period from

Table 1
Characteristics of study population at recruitment (longitudinal cohort) and the general female population aged 18–49 years living in Germany in 2012.

Characteristics	Study population, % (n = 351)	General female population aged 18–49 years, % (n = 16,573,000)[a]
Age group (n = 350)		
18–24 years	9.4	18.4
25–29 years	32.5	14.4
30–34 years	44.2	14.7
35–39 years	12.5	14.0
40–49 years	1.1	38.6
Country of birth (n = 351)		
Germany	94	82.2
Other country	6	17.8
Place of residence[b] (n = 351)		
Eastern Federal States	29.3	18.7
Western Federal States	70.7	81.3
Education level[c] (n = 351)		
Low	1.7	22.0
Middle	17.1	37.5
High	81.2	38.2
Employment (n = 351)		
Not employed	19.7	25.7
Part-time employed	10.5	32.2
Full-time employed	69.8	42.1
Monthly household income (n = 345)		
≤1500 €	12.3	18.4
1501–2000 €	12	11.1
2001–2500 €	14.8	59.2
2501–3000 €	14.8	
≥3001 €	44.4	
Pregnancy trimester (n = 309)		
First	15.1	–
Second	25.9	–
Third	47	–

[a] Data from the microcensus 2012 from the Federal Statistical Office of Germany [32]. Since data concerning household income, age and pregnancy trimester were not available for each woman, data cannot result in 100%.
[b] Eastern Federal States: Mecklenburg-Vorpommern, Brandenburg, Berlin, Saxony, Saxony-Anhalt, Thuringia; Western Federal States: Schleswig-Holstein, Bremen, Hamburg, Lower Saxony, Hesse, Rhineland-Palatinate, Saarland, North Rhine-Westphalia, Bavaria, Baden-Württemberg.
[c] Low: nine years or less of school education; middle: at least 10 years of school education; high: university entrance diploma.

recruitment until child's birthday) before, and a maximum of +426 days (+14 months) after birth.

3.3. Descriptive analysis

S1 Table (supplement) shows means and standard deviations of the main psychological variables and how these change over time. The attitude towards vaccination was relatively positive across all times (M = 82.63, SD = 20.86, range 1–100; 50 represents the neutral midpoint). During all follow-up interviews, the women had higher risk perceptions and worried more about vaccine preventable diseases (VPDs) than about potential vaccine adverse events. It is noteworthy that at recruitment, women rated their own experience with vaccination as rather positive (M = 75.25, SD = 22.98). Later measurements referred to the experience of vaccination with their child, which revealed more negative experiences (M = 50.36, SD = 27.01 when the child was 3 months old). During the final interview, the women were asked to complete the information about their child's vaccination status at age 14 months. N = 216 used their child's vaccination cards and N = 37 recollected the information from memory. When only considering children with information retrieved from vaccination cards, 11.1% were completely vaccinated (i.e., they received all 11 shots as officially recommended at the age of 14 months). Of the 216 children with vaccination cards available, 32.9% had received the recommended four doses of poliovirus-containing vaccines and 29% four doses of pneumococcal conjugate vaccine; 87% had received at least one dose of measles-containing vaccine, 66.7% at least one varicella vaccine dose, and 53.7% a dose of meningococcal C vaccine. None of the women had a completely unvaccinated child. When including also mothers who filled in the questionnaire without the vaccination card at hand, 13 children were unvaccinated (5.1%). On average, children had received 79.01% (SD = 22%; median = 81%) of the recommended vaccines.

3.4. Child's vaccination status

The first analysis explored whether maternal attitudes predicted the completeness of a child's vaccination status. A regression analysis (all variance inflation factors which indicate multicollinearity <2.1; values below 10 are acceptable) predicting the completeness by attitude and controlling for all other determinants showed that attitude at 14 months was the only significant predictor of complete vaccine uptake at 14 months (Table 2). The pattern did not change when controlled for socio-demographic variables. When all mothers (irrespective of whether the vaccination status was recalled from memory or copied from vaccination cards) were included, the influence of attitudes was even stronger ($\beta = .37$, $p < 0.001$; all other $ps > 0.05$). To explore the relation between attitudes at different times and the completeness of the child's vaccination status we correlated the attitudes with vaccination status. It was close to zero at recruitment and increased steadily over time (recruitment $r = 0.09$, $p = 0.192$; 6 months $r = 0.14$, $p = 0.06$, 14 months $r = 0.21$, $p = 0.003$). Further longitudinal analyses are presented below and show the attitude formation process in more detail.

3.5. Development of the attitude over time

The next analyses aimed at analyzing the determinants of attitude development over time. For this purpose, three models were constructed (Table 3). Model 1 predicts attitude changes by variations in risk perceptions and concerns, controlled for changes in vaccination-related knowledge and mothers' own experience with vaccination. Covariance parameters (random effects) revealed that initial intercepts of participants significantly varied across individuals. Over time, attitude scores increased significantly, indicating the development of a more positive attitude over time. Changes in perceived disease risk were not related to changes in the attitude towards vaccination. However, concerns about diseases were associated with positive changes in attitude. Women who increasingly perceived risks associated with VAEs and concerns that vaccines could cause VAEs developed more negative attitudes. Changing from no perceived risk of VAEs to maximum risk would result in a 29% negative change in attitude. Over time, creating positive experiences with vaccination and gaining correct knowledge about vaccination were positively associated with changes in attitude towards vaccination. Controlling for socio-demographic variables did not affect the observed pattern (Table 3, Model 2). Only working part-time as compared to full-time revealed a significant difference of changes in attitude, with part-time employed women developing a less positive attitude compared to full-time employed women. When missing values were imputed, the effect of changes in experience on changes in attitude values was weaker (Model 3). All other predictors remained significant and the pattern remained stable.

As stated in the descriptive data, women's mean perception of their baby's first vaccination was generally less positive than their

Table 2
Multivariate regression on completeness of vaccination status, measured as proportion of recommended vaccinations at the final follow-up interview.

	B	[95% CI]	β	p
Constant	0.40	[0.160, 0.637]		0.001
Attitude	**0.005**	**[0.002, 0.007]**	**0.29**	**0.001**
Risk of disease	0.02	[−0.016, 0.055]	0.08	0.289
Concerns about disease	−0.01	[−0.050, 0.025]	−0.05	0.520
Perceived risk of VAE	0.02	[−0.029, 0.063]	0.07	0.477
Concerns about VAE	0.01	[−0.034, 0.045]	0.02	0.790
Experience	−0.02	[−0.050, 0.009]	−0.09	0.179
Knowledge	−.01	[−0.056, 0.036]	−0.04	0.682
Goodness of Fit	R^2 = .067			
	$F(7, 205) = 2.089$, $p = .05$			

Note: Predictors measured at 14 months after childbirth (n = 212). Significant effect shown in bold.

Table 3
Attitude change over time as a function of changes in perceived risk and concerns, controlled for changes in experience and knowledge (Model 1) and adjusted for socio-economic variables with raw data (Model 2) and imputed data (Model 3).

Goodness of fit	Model 1 (N = 351) −2Log Likelihood = 6906.474			Adjusted Model 2[#] (N = 344) −2Log Likelihood = 6751.091			Imputed adjusted Model 3 (N = 351)		
Fixed effects	B	[95% CI]	P	B	[95% CI]	p	B	[95% CI]	p
Constant	**66.78**	**[61.14, 72.41]**	**0.000**	**67.02**	**[61.26, 72.77]**	**0.000**	**65.94**	**[60.00, 71.87]**	**0.000**
Time	**0.008**	**[0.004, 0.011]**	**0.000**	0.009	[−0.020, 0.038]	0.552	0.013	[−0.018, 0.043]	0.418
Perceived risk of Disease	0.004	[−0.036, 0.044]	0.838	0.005	[−0.036, 0.046]	0.824	0.013	[−0.028, 0.055]	0.533
Concerns about Disease	**0.181**	**[0.142, 0.221]**	**0.000**	**0.182**	**[0.141, 0.222]**	**0.000**	**0.175**	**[0.133, 0.217]**	**0.000**
Perceived risk of VAE	**−0.291**	**[−0.353, −0.229]**	**0.000**	**−0.290**	**[−0.354, −0.236]**	**0.000**	**−0.274**	**[−0.337, −0.211]**	**0.000**
Concerns about VAE	**−0.063**	**[−0.107, −0.020]**	**0.005**	**−0.069**	**[−0.114, −0.025]**	**0.002**	**−0.071**	**[−0.118, −0.025]**	**0.003**
Vaccination-related Experience	**0.055**	**[0.020, 0.091]**	**0.002**	**0.052**	**[0.016, 0.088]**	**0.005**	0.032	[−0.006, 0.071]	0.098
Vaccination-related Knowledge	**0.160**	**[0.112, 0.207]**	**0.000**	**0.160**	**[0.111, 0.209]**	**0.000**	**0.185**	**[0.136, 0.235]**	**0.000**
Employment*Time									
Not employed	–		–	0.000	[−0.010, 0.010]	0.990	−0.002	[−0.012, 0.008]	0.715
Part-time employed	–		–	**−0.014**	**[−0.025, −0.003]**	**0.010**	**−0.013**	**[−0.025, −0.003]**.	**0.012**
Full-time employed	–		–	Ref.	–	–	Ref.	–	–
Age * Time									
18–24 years	–		–	−0.009	[−0.038, 0.020]	0.545	−0.009	[−0.040, 0.021]	0.544
25–29 years	–		–	−0.000	[−0.026, 0.026]	0.992	−0.003	[−0.030, 0.024]	0.809
30–34 years	–		–	0.006	[−0.020, 0.032]	0.637	0.003	[−0.024, 0.029]	0.839
35–39 years	–		–	0.008	[−0.020, 0.035]	0.580	0.003	[−0.024, 0.031]	0.806
40–49 years	–		–	Ref.	–	–	Ref.	–	–
Education * Time[+]									
Low	–		–	0.014	[−0.011, 0.040]	0.276	0.024	[−0.001, 0.050]	0.061
Middle	–		–	0.002	[−0.008, 0.011]	0.730	0.004	[−0.005, 0.013]	0.436
High	–		–	Ref.	–	–	Ref.	–	–
Income (€) * Time									
≤1500	–		–	0.008	[−0.005, 0.020]	0.224	0.003	[−0.010, 0.015]	0.664
1501–2000	–		–	0.011	[−0.001, 0.022]	0.058	0.009	[−0.002, 0.020]	0.105
2001–2500	–		–	0.006	[−0.004, 0.017]	0.219	0.003	[−0.007, 0.013]	0.511
2501–3000	–		–	0.007	[−0.003, 0.017]	0.148	0.005	[−0.004, 0.015]	0.270
≥3000	–		–	Ref.	–	–	Ref.	–	–
Random effects		Wald Z	p		Wald Z	P			
Intercept		**6.12**	**.000**		**5.85**	**0.000**			

Note: An AR(1) covariance structure was used for residuals of all models. A UN covariance structure was initially used for random effects in all models. However, models including random slopes did not converge due to a lack of variance. Final models presented are with random intercept only (scaled covariance structure). Significant results are highlighted in bold. X^1*X^2 indicates an interaction term between X^1 and X^2.

[#] Other non-significant results of this model were country of birth and place of residence.

[+] Low: nine years or less of school education; middle: at least 10 years of school education; high: university entrance diploma. Interpretation: A one-point increase in concerns about diseases (measured on a scale ranging from 0 to 100) results in about 0.18% increase of the attitude score, indicating a more positive attitude. For experience, a change of 1 point (0–100) increases the attitude by 0.055%. Increasing knowledge by 1 unit on the POMP scale results in about 0.16% increase of attitude scores (note that one unit of the knowledge test corresponds to 11.11 POMP units). All other scores can be interpreted likewise.

previous experiences. The previous analysis has shown that changes in experience are an important predictor. The violin plots in Fig. 3 therefore visualize the influence of the first vaccination experience on attitude development. The panels present data of women whose first childhood vaccination experience was worse (upper panel A) or equal to or better than previous own experiences (lower panel B). The figure demonstrates that when the first experience was equal or better than previous experiences (B), all women had generally positive attitudes (over the midpoint of the attitude scale) when their child was 14 months old. When the experience was worse, there was no such positive development. The interaction effect (repeated measurement ANOVA with attitude and experience as factors) was significant ($F(1,166) = 4.84$, $p < 0.05$).

As previous work has shown that repeated expression of attitudes can lead to more extreme attitudes [15], we tested whether attitudes in the longitudinal cohort differed from the control cohorts. In no case was attitude significantly different in the cross-sectional control cohorts compared to the appropriate longitudinal cohort ($M_{long6} = 82.2$, 95%CI: 79.7–84.6; $M_{cross6} = 81.5$, 95%

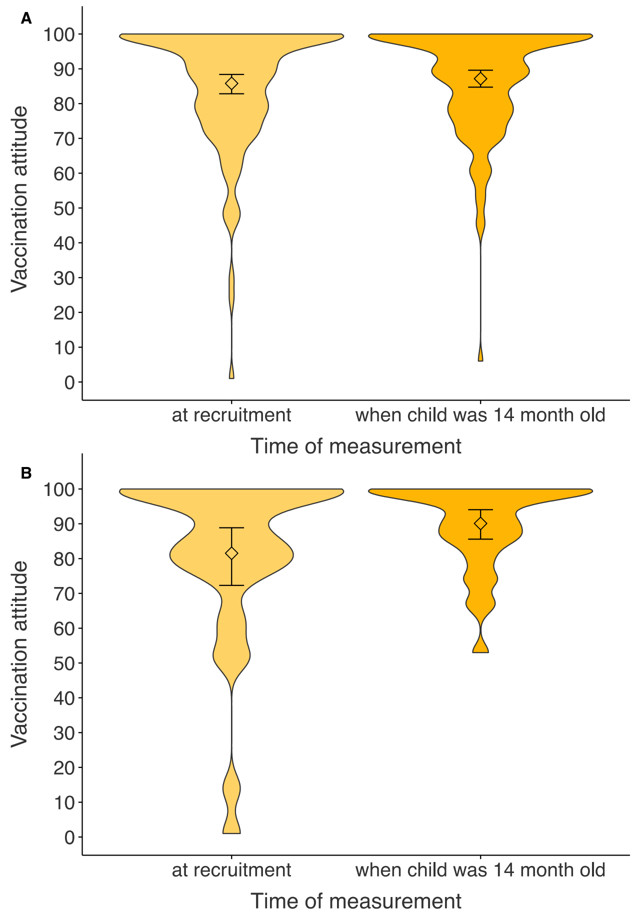

Fig. 3. Violin plots of the vaccination attitude at recruitment and when the child was 14 months old depending on experiences with childhood vaccinations (A: first experience with childhood vaccination was worse than prior own vaccination experiences, B: first experience with childhood vaccination was equal to or better than prior own experiences). Note: In this violin plots the diamonds represents the mean values, the whiskers the 95%CIs of the mean, the curves represent the density function. The upper panel (A) shows data of women whose experiences with their child's first vaccination were worse than their prior own experiences with vaccination. In this case, both at recruitment and when the child was 14 months, the attitude towards vaccination is distributed across the whole spectrum. The mean attitude towards vaccination does not change significantly ($F(1, 135)<1$). The lower panel (B) shows that when the experiences with their baby's first vaccination were equal to or better than prior experiences, the attitude becomes more positive ($F(1,31) = 6.46$, $p < 0.05$) and women with negative prior attitudes shift their attitude to the more positive end of the scale, which is indicated by the changes in the distribution. The interaction effect (repeated measurement ANOVA with attitude and experience as factors) is significant ($F(1,166) = 4.84$, $p < 0.05$). Subsample of n = 168 (complete data for all relevant variables at recruitment and at 14 months).

CI: 78.8–84.3; M_{long14} = 83.8, 95%CI: 81.1–86.5; $M_{cross14}$ = 81.7, 95% CI: 78.5–84.9).

3.6. Development of perceived risk of and concerns about VAEs over time

The next analyses aimed at shedding light on how risk perceptions and concerns about vaccine adverse events (VAE) increase and decrease over time. Table 4 shows the influence of vaccination-related experiences and knowledge on perceived risk of and concerns about VAEs. Over the study period, holding misinformation led to higher risk perception. Specifically, being wrong on one item in the 9 item knowledge test results in a 4.08% (0.367 $*$ 11.11) increase of perceived risk of VAE and 4.8% (0.44 $*$ 11.11) increased level of concern (one unit of the knowledge test corresponds to 11.11 POMP units). Importantly, making positive experiences with vaccination reduced the perceived risk of VAEs and the concerns about VAEs. Again, controlling for socio-demographic variables and imputing missing values did not change the pattern of the results (Tables S3 and S4 in the Supplement).

3.7. Changes in knowledge

As knowledge was an important predictor of risk perceptions, the following analysis aimed at identifying relevant sources that increase correct vaccine-related knowledge. Table 5 shows the results of a mixed-effects regression predicting changes in knowledge as a function of changing relevance of different sources. Physicians were the most influential source of knowledge. Regressing changes in knowledge on changes in relevance of different sources revealed that when physicians and television became more relevant over time, the women had higher knowledge scores. When midwives and books became more relevant, knowledge about vaccination decreased significantly. When controlling for socio-demographic factors, the effect of midwives was weakened. Moreover, the analysis revealed a significant effect of medium level of education: women with a maximum of 10 years of school were less knowledgeable about vaccination than more highly educated women. This effect and the effects of the relevance of midwives and television were non-significant when missing values were imputed (S5 Table).

Having participants answer "true-false" statements repeatedly may make the false statements more accessible in memory and thus more credible [16]. However, comparison of knowledge in the longitudinal cohort to the control cohorts showed that repeated assessment of knowledge did not lead to increases in misconceptions (see Supplement).

4. Discussion

Our study confirms that maternal attitudes towards vaccination are a critical factor in predicting the child's vaccine uptake. While attitudes during pregnancy were not correlated with the child's vaccination status at age 14 months, attitudes become more meaningful for vaccination behavior as the child becomes older. The findings demonstrate that the first vaccination experiences a mother has with her child as well as information acquired during the first year of life are crucial. The cascade of analyses traces back the development of the attitude to increasing concerns about the disease and perceived risks and concerns about VAEs. These increases in perceived vaccination-related risks and concerns were both related to more negative experiences.

A potential pathway of a negative vaccination attitude could be a woman who actually has a positive attitude towards vaccination before giving birth, but has a negative experience with the first vaccine shot of her child (e.g. due to the feeling that the baby was hurt, crying of the baby due to pain, feeling overwhelmed by the situation, etc.) [17]. These experiences may then lead to concerns about vaccine safety and information searches, which quite likely will also include anti-vaccination sources [18]. Thus, even though the initial attitude was positive, making negative experiences may instigate processes of attitude development that lead to subsequent under-vaccination of the child.

Under-vaccination can be the result of either delaying or completely refusing certain vaccines. In our population, most under-vaccinated children at the age of 14 months missed the fourth dose of poliovirus-containing or the fourth dose of pneumococcal conjugate vaccine. Longitudinal analyses of birth cohorts in Germany have shown that in particular the 4th dose of poliovirus-containing vaccines (usually given as a hexavalent formulation)

Table 4
Changes over time in perceived risk of VAE and concerns about VAE as a function of changes in knowledge and experiences with vaccination.

Goodness of fit	Perceived risk of VAE (N = 351) −2Log Likelihood = 9069.408			Concerns about VAE (N = 351) −2Log Likelihood = 9912.458		
Fixed effects	*B*	[95% CI]	*p*	*B*	[95% CI]	*p*
Constant	**57.09**	**[53.37, 60.82]**	**0.000**	**81.87**	**[76.46, 87.27]**	**0.000**
Time	0.000	[−0.004, 0.005]	0.880	0.003	[−0.003, 0.010]	0.279
Experience	**−0.087**	**[−0.122, −0.052]**	**0.000**	**−0.167**	**[−0.219, −0.115]**	**0.000**
Knowledge	**−0.367**	**[−0.412, −0.323]**	**0.000**	**−0.446**	**[−0.511, −0.381]**	**0.000**
Random Effects		*Wald Z*	*p*	*Wald Z*	*p*	
Intercept		7.09	0.000	7.10	0.000	
Slope		1.32	0.188	–	–	

Note: An AR(1) covariance structure was used for residuals of all models. A UN covariance structure was used for random effects in all models. Significant results are highlighted in bold. The model analyzing concerns about VAE did not converge including random slope. Therefore the model was reduced to a random intercept only model.

Table 5
Changes in knowledge as a function of changes in source relevance, (un)adjusted for socio-demographic factors.

Goodness of fit	Unadjusted model (N = 309) −2Log Likelihood = 5686.708			Adjusted model[#](N = 303) −2Log Likelihood = 5556.326		
Fixed effects	*B*	[95% CI]	*p*	*B*	[95% CI]	*p*
Constant	**58.21**	**[51.22, 65.20]**	**0.000**	**57.18**	**[51.01, 65.35]**	**0.000**
Time	**−0.010**	**[−0.018, −0.002]**	**0.019**	0.029	[−0.033, 0.091]	0.355
Relevance of Source						
Physician	**0.349**	**[0.232, 0.466]**	**0.000**	**0.351**	**[0.231, 0.470]**	**0.000**
Midwife	**−0.107**	**[−0.200, −0.014]**	**0.025**	−0.094	[−0.190, −0.001]	0.053
Television	**0.142**	**[0.007, 0.277]**	**0.039**	**0.155**	**[0.017, 0.294]**	**0.028**
Books	**−0.121**	**[−0.219, −0.024]**	**0.015**	**−0.135**	**[−0.234, 0.036]**	**0.008**
Internet	−0.015	[−0.137, 0.107]	0.807	−0.014	[−0.138, 0.110]	0.825
Courses	−0.130	[−0.284, 0.025]	0.100	−0.105	[−0.263, 0.053]	0.193
Family	−0.040	[−0.143, 0.063]	0.447	−0.049	[−0.154, 0.055]	0.354
Newspaper	0.077	[−0.044, 0.199]	0.213	0.070	[−0.054, 0.193]	0.268
Pharmacist	0.029	[−0.091, 0.149]	0.638	−−0.031	[−0.092, 0.154]	0.623
Internet Forums	−0.106	[−0.229, 0.015]	0.088	−0.107	[−0.232, −0.018]	0.094
Social Media	−0.194	[−0.433, 0.046]	0.112	−0.202	[−0.447, 0.042]	0.104
Age * Time						
18– 24 years	–		–	−0.029	[−0.092, 0.033]	0.357
25–29 years	–		–	−0.025	[−0.082, 0.032]	0.380
30– 34 years	–		–	−0.023	[−0.079, 0.033]	0.417
35– 39 years	–		–	−0.017	[−0.075, 0.042]	0.573
40–49 years	–		–	Ref.	–	–
Education[+] * Time						
Low	–		–	−0.035	[−0.093, 0.023]	0.232
Middle	**–**		**–**	**−0.023**	**[−0.044, −0.001]**	**0.043**
High	–		–	Ref.	–	–
Income (€) * Time						
≤1500	–		–	−0.010	[−0.035, 0.015]	0.434
1501–2000	–		–	−0.018	[−0.040, 0.004]	0.104
2001–2500	–		–	−0.009	[−0.029, 0.011]	0.359
2501–3000	–		–	−0.000	[−0.021, 0.021]	0.977
≥3000	–		–	Ref.	–	–
Random Effects		*Wald Z*	*p*		*Wald Z*	*p*
Intercept		6.64	0.000		6.26	0.000
Slope		1.27	0.204		0.992	0.321

Note: An AR(1) covariance structure was used for residuals of all models. A UN covariance structure was initially used for random effects in all models. However, model 1 including random slopes did not converge due to a lack of variance. Results of model 1 are presented with random intercept only (scaled covariance structure). Significant results are highlighted in bold. $X^1 * X^2$ indicates an interaction term between X^1 and X^2.

[#] Other non-significant results of this model were employment, country of birth and place of residence.

[+] Low: nine years or less of school education; middle: at least 10 years of school education; high: university entrance diploma.

is often delayed and a considerable uptake still takes place until the age of 36 months or even later [19].

4.1. Practical implications

The results of the study have several implications for future policymaking and vaccine advocacy. First, education about vaccination should start as early as during pregnancy [20–22]. This study showed that attitudes are not yet predictive for vaccine uptake later on. Thus, even a mother with a negative attitude during pregnancy may end up with a well-vaccinated child, depending on her experience with vaccination as well as the information she acquired. These determine how the attitude develops and whether mothers decide for or against vaccination. Second, doctors should play a central role in educating pregnant women on vaccination-related issues as their influence is highly relevant and significant. A study showed that although pregnant women are interested in childhood vaccine information, the majority of them had not received any from their physician or midwife, and if so, many were not satisfied with the information received [20]. Regular pregnancy check-ups could be utilized for discussing vaccinations. Additionally, another chance for education might be maternal vaccinations (e.g. against influenza, pertussis), as one of the reasons behind the vaccines are passing on protection for the newborn's first few months of life. This way, doctors can take the opportunity to introduce the topic of childhood immunization as early as during pregnancy. Introducing the idea of protecting others has been shown to increase the willingness to vaccinate [23], so educating about childhood vaccination and the protection of others has several benefits. Finally, making vaccination of the child a positive experience is crucial. In accordance with the results of this study, Nowak and Cacciatore [24] also showed that personal experience of bad or adverse events was associated with lower vaccine confidence. With the newborn, it is therefore important to create opportunities for positive vaccination experiences. While mothers in our study population had rather positive experiences with vaccination themselves, it was remarkable that the experiences with the child were rated as far less positive. Reducing pain of the injection and stressful experiences during the procedure could be one possibility. There are several evidence-based sets of recommendations for reducing pain and stress connected with vaccinations. These include certain injection procedures, distraction or use of topical anesthetics that can reduce the pain of vaccination [17,25–27]. Additionally, providing guidance to parents about how to deal with (potentially first) fever could increase parents' self-efficacy and experience in dealing with the vaccination situation.

4.2. Strength and limitations

The major strength of this study is the longitudinal cohort design as it facilitates analyzing the determinants of attitude development over time. Additionally, cross-sectional control groups increased the internal validity, as the influence of repeated participation (especially on knowledge and attitude) can generally be ruled out. The imputed data correcting for missing values yielded almost the same pattern of results.

A limitation is a potential selection bias regarding the study sample. In the advertisements for recruitment the study was framed as being concerned with health issues. Women who are especially interested in health topics and who may also have an especially positive attitude regarding vaccination may be overrepresented. The overall attitude was indeed quite positive. Pro-vaccination indicators (high knowledge, no safety concerns) also led to a higher probability of participation at later interviews (see Supplement). However, there was no systematic bias identified for women with a particular positive or negative attitude to drop out of the study (see Supplement). Nevertheless, the overall positive attitude could indicate a potential bias with vaccine-critical individuals being underrepresented in the study. However, in Germany [28] and other countries [29] the attitude towards vaccination is left-skewed with only a relatively small proportion of parents being absolutely against vaccination. The positive attitude did not evolve through repeated participation as comparisons with the control groups revealed. In addition, our sample was more highly educated than would be expected in a representative sample. Having recruited women with higher education status might be also responsible for the higher employment of the women and the higher total income. This may in total impact the absolute and relative relevance of the sources of information. However, in general our results did not reveal an association between attitude and education status.

The results pertain to women only. However, the decision process may be a shared one – not only between the mother and the physician, but also the father of the child. Medical decision processes within a partnership are rarely investigated [30]. Research has identified the mother as the main decision-maker regarding childhood vaccination [31]; however, the gap between a positive attitude and actual vaccination behavior may be attributable at least partially to compromise between the parents. Thus, future research should also consider the role of fathers and the fathers' experiences with childhood vaccination in this process. Additionally, future research should identify ways to scaffold the developmental process of the maternal attitude. RCTs should systematically change the identified determinants (i.e. improve the first vaccination experience) and assess their causal effects on attitude development.

5. Conclusion

This study adds knowledge about the developmental process of maternal attitudes towards vaccination. The data suggest that the experience made during the first vaccination of their child is related to changes in risk perceptions and concerns about vaccination, which are most strongly related to changes in the maternal attitude towards vaccination. Understanding this pathway of attitude development allows the prevention of vaccine hesitancy as early as during pregnancy: following up mothers' own positive experiences by creating new positive experiences with vaccinating the newborn should lead to the development of a more positive attitude towards vaccination.

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Conflicts of interest

None.

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Data sharing

The full data set and the imputed data set are available at *https://osf.io/chk97/*. Consent for data sharing was not obtained by the participants but the presented data are anonymized and identification is not possible.

Competing interests

All authors state that they have no conflicts of interests.

Ethical approval

Ethical approval was obtained from the Ethics Committee of the Charité, Berlin (EA1/010/12).

Contributors' statement

CB is guarantor for this study; initiated the collaborative project; designed questionnaire; monitored data collection for the whole trial; analyzed the data; drafted the paper.

BB monitored data collection for the whole trial; cleaned and analyzed the data; drafted the paper.

PS wrote the statistical analysis plan; cleaned and analyzed the data; drafted the paper.

OW initiated the collaborative project; drafted the paper.

All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2018.04.023.

References

[1] Dubé E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger JA. Vaccine hesitancy: an overview. Hum Vaccines Immunother 2013;9:1763–73. https://doi.org/10.4161/hv.24657.
[2] MacDonald NE, Working SAGE. Group on vaccine hesitancy. Vaccine hesitancy: definition, scope and determinants. Vaccine 2015;33:4161–4. https://doi.org/10.1016/j.vaccine.2015.04.036.
[3] Schmid P, Rauber D, Betsch C, Lidolt G, Denker M-L. Barriers of influenza vaccination intention and behavior – a systematic review of influenza vaccine hesitancy, 2005–2016. PLOS One 2017;12:e0170550. https://doi.org/10.1371/journal.pone.0170550.
[4] Betsch C, Böhm R, Chapman GB. Using behavioral insights to increase vaccination policy effectiveness. Policy Insights Behav Brain Sci 2015;2:61–73.
[5] Ajzen I. The theory of planned behavior. ResearchGate 1991;50:179–211. https://doi.org/10.1016/0749-5978(91)90020-T.
[6] Hofman R, van Empelen P, Richardus JH, de Kok IMCM, de Koning HJ, van Ballegooijen M, et al. Predictors of HPV vaccination uptake: a longitudinal study among parents. Health Educ Res 2014;29:83–96. https://doi.org/10.1093/her/cyt092.
[7] Opel DJ, Mangione-Smith R, Taylor JA, Korfiatis C, Wiese C, Catz S, et al. Development of a survey to identify vaccine-hesitant parents: the parent attitudes about childhood vaccines survey. Hum Vaccin 2011;7:419–25.
[8] American Academy of Arts and Sciences. Public Trust in Vaccines: Defining a Research Agenda. Cambridge, Mass.: American Academy of Arts and Sciences; 2014.
[9] Kobbeltvedt T, Wolff K. The Risk-as-feelings hypothesis in a Theory-of-planned-behaviour perspective. Judgm Decis Mak 2009 2009; 4(7): 567–86.
[10] van der Linden S. On the relationship between personal experience, affect and risk perception: the case of climate change: personal experience, affect and risk perception. Eur J Soc Psychol 2014;44:430–40. https://doi.org/10.1002/ejsp.2008.
[11] Ständige Impfkommission. Empfehlungen der Ständigen Impfkommission (STIKO) am Robert Koch-Institut/Stand: Juli 2011. Epid Bull 2011;30:275–94.
[12] Bödeker B, Betsch C, Wichmann O. Skewed risk perceptions in pregnant women: the case of influenza vaccination. BMC Public Health 2015;15:1.
[13] Betsch C, Bödeker B, Schmid P, Wichmann O. Materials and Data of The development of the maternal attitude towards vaccination – a prospective cohort study n.d. <https://osf.io/chk97/>.
[14] Cohen P, Cohen J, Aiken LS, West SG. The problem of units and the circumstance for POMP. Multivar Behav Res 1999;34:315–46. https://doi.org/10.1207/S15327906MBR3403_2.
[15] Downing JW, Judd CM, Brauer M. Effects of repeated expressions on attitude extremity. J Pers Soc Psychol 1992;63:17–29. https://doi.org/10.1037/0022-3514.63.1.17.
[16] Lewandowsky S, Ecker UKH, Cook J. Beyond misinformation: understanding and coping with the "post-truth" era. J Appl Res Mem Cogn 2017;6:353–69. https://doi.org/10.1016/j.jarmac.2017.07.008.
[17] Reducing pain at the time of vaccination. WHO position paper, september 2015—Recommendations. Vaccine 2016;34:3629–30. https://doi.org/10.1016/j.vaccine.2015.11.005.
[18] Kata A. Anti-vaccine activists, Web 2.0, and the postmodern paradigm–An overview of tactics and tropes used online by the anti-vaccination movement. Vaccine 2012;30:3778–89.
[19] Rieck T, Feig M, Eckmanns T, Benzler J, Siedler A, Wichmann O. Vaccination coverage among children in Germany estimated by analysis of health insurance claims data. Hum Vaccines Immunother 2014;10:476–84. https://doi.org/10.4161/hv.26986.
[20] Weiner JL, Fisher AM, Nowak GJ, Basket MM, Gellin BG. Childhood immunizations. Vaccine 2015;33:D92–8. https://doi.org/10.1016/j.vaccine.2015.09.037.
[21] Saitoh A, Nagata S, Saitoh A, Tsukahara Y, Vaida F, Sonobe T, et al. Perinatal immunization education improves immunization rates and knowledge: a randomized controlled trial. Prev Med 2013;56:398–405. https://doi.org/10.1016/j.ypmed.2013.03.003.
[22] Gagneur A., Dubé È., Farrands A., Lemaître T., Boulianne N., Sauvageau C. et al. Promoting vaccination at birth with motivational interviewing session improves vaccination intention and reduces vaccination hesitancy. Eur Soc Paediatr Infect Dis Brighton UK May 15th 2016 n.d.
[23] Betsch C, Böhm R, Korn L, Holtmann C. On the benefits of explaining herd immunity in vaccine advocacy. Nat Hum Behav. 2017.
[24] Nowak GJ, Cacciatore MA. Parents' confidence in recommended childhood vaccinations: Extending the assessment, expanding the context. Hum Vaccines Immunother 2017;13:687–700. https://doi.org/10.1080/21645515.2016.1236881.
[25] Taddio A, McMurtry CM, Shah V, Riddell RP, Chambers CT, Noel M, et al. Reducing pain during vaccine injections: clinical practice guideline. Can Med Assoc J 2015;187:975–82. https://doi.org/10.1503/cmaj.150391.
[26] Boerner KE, Birnie KA, Chambers CT, Taddio A, McMurtry CM, Noel M, et al. Simple psychological interventions for reducing pain from common needle procedures in adults: systematic review of randomized and quasi-randomized controlled trials. Clin J Pain 2015;31:S90–8. https://doi.org/10.1097/AJP.0000000000000270.
[27] Koch-Institut R. Empfehlungen der Ständigen Impfkommission (STIKO) am RKI Stand: August 2016. RKI-Bib1 (Robert Koch-Institut); 2016. http://doi.org/10.17886/EpiBull-2016-051.4.
[28] für gesundheitliche Aufklärung. Elternbefragung zum Thema "Impfen im Kindesalter"–Ergebnisbericht. Köln. 2011.
[29] Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, et al. The state of vaccine confidence 2016: global insights through a 67-country survey. EBioMed 2016;12:295–301. https://doi.org/10.1016/j.ebiom.2016.08.042.
[30] Lewis MA, McBride CM, Pollak KI, Puleo E, Butterfield RM, Emmons KM. Understanding health behavior change among couples: an interdependence and communal coping approach. Soc Sci Med 2006;62:1369–80. https://doi.org/10.1016/j.socscimed.2005.08.006.
[31] Berenson AB, Laz TH, Hirth JM, McGrath CJ, Rahman M. Effect of the decision-making process in the family on HPV vaccination rates among adolescents 9?17 years of age. Hum Vaccines Immunother 2014;10:1807–11. https://doi.org/10.4161/hv.28779.
[32] German Federal Statistical Office. Mikrozensus 2012. n.d. <https://www.destatis.de>.