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Immunity against measles, mumps, rubella, varicella, diphtheria, tetanus, polio, hepatitis A and hepatitis B among adult asylum seekers in the Netherlands, 2016

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ABSTRACT

Asylum seekers are a vulnerable population for contracting infectious diseases. Outbreaks occur among children and adults. In the Netherlands, asylum seeker children are offered vaccination according to the National Immunization Program. Little is known about protection against vaccine-preventable diseases (VPD) in adult asylum seekers. In this 2016 study, we assessed the immunity of adult asylum seekers against nine VPD to identify groups that might benefit from additional vaccinations. We invited asylum seekers from Syria, Iran, Iraq, Afghanistan, Eritrea and Ethiopia to participate in a serosurvey. Participants provided informed consent and a blood sample, and completed a questionnaire. We measured prevalence of protective antibodies to measles, mumps, rubella, varicella, diphtheria, tetanus, polio type 1–3 and hepatitis A and B, stratified them by country of origin and age groups. The median age of the 622 participants was 28 years (interquartile range: 23–35), 81% were male and 48% originated from Syria. Overall, seroprotection was 88% for measles (range between countries: 83–93%), 91% for mumps (81–95%), 94% for rubella (84–98%), 96% for varicella (92–98%), 82% for diphtheria (65–88%), 98% for tetanus (86–100%), 91% (88–94%) for polio type 1, 95% (90–98%) for polio type 2, 82% (76–86%) for polio type 3, 84% (54–100%) for hepatitis A and 27% for hepatitis B (anti-HBs; 8–42%). Our results indicate insufficient protection against certain VPD in some subgroups. For all countries except Eritrea, measles seroprotection was below the 95% threshold required for elimination. Measles seroprevalence was lowest among adults younger than 25 years. In comparison, seroprevalence in the Dutch general population was 96% in 2006/07. The results of this study can help prioritizing vaccination of susceptible subgroups of adult asylum seekers, in general and in outbreak situations.

1. Introduction

In recent years there has been a large influx of refugees in Europe. In several countries of origin, public health systems collapsed and vaccination programmes have been interrupted due to war, political or economic instability, resulting in inconsistent vaccination coverage among refugee populations [1]. In the EU, outbreaks and isolated cases of several vaccine-preventable diseases (VPD), such as measles [2], hepatitis A [3,4], varicella [5] and diphtheria [6], have been reported among both children and adult refugees.

The World Health Organization recommends vaccination of refugees, asylum seekers and migrants according to the host countries' vaccination programme if they intend to stay in a country for more than one week. Considering the outbreak potential, vaccination against measles, mumps and rubella (MMR), as well as polio should be prioritized [7]. In the Netherlands, the vaccination status of asylum seeker children and adolescents aged 0–18 years is evaluated within 6 weeks after arrival, and vaccinations are updated according to the national immunization program (NIP) [8]. The vaccination status of adult asylum seekers however is not routinely

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evaluated. Two recent serosurveys from Germany found that immunity among adult asylum seekers was relatively high but might still be insufficient to achieve herd immunity for measles, mumps, rubella, varicella and diphtheria [9–11].

We conducted a seroprevalence survey in the Netherlands among adult asylum seekers to determine the seroprevalence against nine VPDs. By identifying immunity gaps and potential vaccination needs among adult asylum seekers, results of this study can aid the development of vaccination policies for asylum seekers.

2. Materials & methods

2.1. Study design

In July and August 2016, we performed a cross sectional serological survey among adult asylum seekers living in three large reception centres in The Netherlands.

2.2. Study population

Asylum seekers that met the following inclusion criteria were eligible to participate in the study: (i) 18 to 45 years of age, (ii) originating from Syria, Iran, Iraq, Afghanistan, Eritrea and Ethiopia, and (iii) living in a reception centre in the Netherlands. We chose this age range based on these reasons: insufficiently vaccinated asylum seeker children below the age of 19 years are already offered vaccination in the Netherlands and persons above the age of 45 years are more likely to have protective antibody levels due to natural infection [9]. Also, the majority of adult asylum seekers housed in Dutch reception centres were younger than 45 years (>80%) [12]. The countries we selected represented the countries where most asylum seekers in The Netherlands originated from in 2015 [13].

2.3. Participant recruitment

The Central Agency for the Reception of Asylum Seekers (COA) is responsible for the reception of asylum seekers and offers housing during the (first) asylum procedure. In consultation with COA, three reception centres were selected as study sites based on convenience regarding travel distance and size of the centre. These three centres housed ~1750 (8%) asylum seekers of the ~22,000 asylum seekers present in the Netherlands who met the inclusion criteria (personal communication COA, data as on 1-2-2016). One week prior to data collection, eligible participants received an invitation letter in Arabic, Farsi, Tigrinya, Amharic, Dutch or English. A flyer with icons describing the study graphically was included to also reach illiterate asylum seekers. Posters with information about the study were placed in the communal areas. In addition, personnel from the centres orally informed eligible study participants.

2.4. Data collection

Two to four consecutive sampling days were held at each centre in July and August 2016. On these sampling days, interpreters (Arabic, Farsi, Tigrinya and Amharic) explained the study aim and procedures to eligible persons, and assisted with filling in the informed consent form and the questionnaire. The questionnaire contained questions about demographics (sex, age, country of birth, educational level according to the UNESCO International Standard Classification of Education), and whether the person grew up in an urban or rural environment. Also, participants were asked whether they had received vaccinations as a child, and whether they would accept any future vaccination if indicated and offered to them in the Netherlands. To prevent potentially lower participation of women due to cultural reasons, we specifically recruited female nurses to collect a blood sample from all participants (8.5 mL, BD Vacutainer® SSTTM II Advance tubes). All data were processed anonymously: the questionnaire and blood sample were labelled with a unique study number and no person identifiable information was collected.

2.5. Serological analysis

After sample collection, blood samples were kept at room temperature. Upon transfer to the National Institute for Public Health and the Environment at the end of the sampling day, samples were stored in the refrigerator until further processing the next morning. After centrifugation, serum aliquots were filled out and were stored at −20 °C.

IgG antibodies against measles-, mumps-, rubella- and varicella virus, and diphtheria and tetanus were determined using fluorescent bead-based multiplex immunoassay (Luminex xMAP technology), as described before [14,15]. In all assays a reference, controls and blanks were included on each plate. All analysis was performed with a Bio-Plex 200 in combination with Bio-Plex manager software (Bio-Rad Laboratories, Hercules, CA).

Hepatitis A and hepatitis B (markers: anti-HBc, HBsAg, anti-HBs) serology was performed using chemoluminescence assays performed on the ADVIA Centaur XP assay system (Siemens HBsAgII assay, HBcT, aHBs2, AHAVT). A positive test result for HBsAg was confirmed by a neutralisation assay (Siemens) and/or by PCR (COBAS Taqman, Roche).

Poliovirus neutralising antibody titres against serotypes 1, 2, and 3 were determined by the neutralisation test (NT) using Sabin vaccine strains, as recommended by the WHO [16].

Participants were considered protected when IgG concentrations were above or equal to the following disease-specific cut offs: ≥0.20 IU/mL for measles, ≥45 IU/mL for mumps, ≥10.0 IU/mL for rubella, 0.26 IU/mL for varicella, ≥0.01 IU/mL for diphtheria, ≥0.01 IU/mL for tetanus, ≥20 mIU/mL for hepatitis A and >10 mIU/mL for hepatitis B (anti-HBs). For hepatitis B, vaccine-induced immunity is defined as anti-HBs positivity without other markers. Anti-HBc-, in combination with anti-HBs-positivity indicates a resolved infection with immunity, while anti-HBc positivity with presence of HBsAg indicates a chronic infection. For poliovirus NT titres ≥8 were considered protective. For diphtheria and tetanus protective immunity was further subdivided into basic protection (0.01–0.099 IU/mL) and full protection (≥0.1 IU/mL). Hereafter, we refer to seroprevalence of protective antibody levels as seroprevalence.

2.6. Statistical analyses

Serological results for measles, mumps, rubella and varicella were available for all study participants (n = 622). For diphtheria, tetanus, and hepatitis A, seroprevalence results were available for 620 participants and for hepatitis B for 617 participants, respectively. Due to limited resources, we only tested a subset of samples (n = 300, 48%) for the presence of antibodies against polio virus types 1–3. We used SPSS (IBM Corp, version 24) to determine the subset of samples, that constituted of a random selection of 100 sera from Syrian participants (as this was the largest group), and 50 sera each from participants from other eligible countries.

We calculated seroprevalences, determined exact 95% confidence intervals (Clopper Pearson) and stratified seroprevalence between gender, age groups (18–25, 26–35, 36–45) and country of birth using Chi square tests or Fisher's exact tests. For the comparisons of seroprevalence between countries of birth, we excluded participants from Ethiopia due to the low sample size (n = 2). To investigate trends in seroprevalence between age groups, we used the Cochrane Armitage Trend test. We tested

whether observed seroprevalence for measles, mumps, rubella, varicella, diphtheria and polio were statistically significantly below established herd immunity thresholds by using one-tailed one-sample z-tests for proportion. For measles and rubella, we used the WHO threshold of 95% required for measles and rubella elimination [17]. We used the upper limits of the herd immunity thresholds determined by Plans Rubio et al., for varicella (91%), mumps (93%), diphtheria (80%) and polio (86%) as thresholds for seroprevalence. [18]. Subgroups within the study population were considered insufficiently protected when their age- and country-specific seroprevalence was significantly below these thresholds. A p-value (P) of 0.05 was considered statistically significant.

Data analysis was conducted in Stata (StataCorp LP, Texas, USA, version 14.2). Figures were made in RStudio (R studio Inc., Boston, MA, USA, version 0.99.903) using the package 'ggplot2'.

2.7. Ethics

This study was approved by the Medical Ethical Committee Noord-Holland (number: M016-010/ NL56277.094.16). Potential participants were informed that their asylum procedure would not be influenced by (non)participation or by the test results, and that participants would not receive their test results. All participants provided written informed consent. Data collection and analysis was anonymous.

3. Results

In total, 637 adult asylum seekers participated in the study. Fifteen participants were excluded from the final analysis: 10 participants did not meet the inclusion criteria (two fell outside the defined age range and eight originated from countries other than those specified) and from five participants no blood sample could be taken.

The final study population comprised of 622 participants: 297 were from Syria, 109 from Iran, 83 from Iraq, 75 from Afghanistan, 56 from Eritrea and 2 from Ethiopia, respectively. Table 1 shows the characteristics of the study population. The median age of all study participants was 28 years (IQR: 23–35) and 81% were male (Table 1). Ages were comparable between men (median: 28, IQR: 23–35) and women (median: 29, IQR: 25–35 (p = 0.301). Of the 622 participants, 552 (89.5%) reported having a positive attitude towards future vaccinations, 20 were opposed (3.2%) and 45 did not know (7.3%). Five participants did not answer the question.

Table 1
Characteristics of adult asylum seekers that participated in the serosurvey (n = 622), The Netherlands, July–August 2016

	Characteristic	n	%
Gender	Male	504	81.0
	Female	117	18.8
	Missing	1	0.2
Age group	18–25	203	32.6
	26–35	274	44.1
	36–45	145	23.3
Country of birth	Syria	297	47.8
	Iran	109	17.5
	Iraq	83	13
	Afghanistan	75	12
	Eritrea	56	9
	Ethiopia	2	0.3
Environment grow up	Rural	106	17
	Urban	505	81.2
	Missing	11	2
Highest level of education	Primary school	188	30.2
	Secondary school	216	34.7
	Intermediate	67	11
	University/college	145	23.5
	Missing	5	1
Self-reported childhood vaccinations	Yes	526	84.6
	No	15	2
	Do not know	74	12
	Missing	7	1

3.1. Seroprevalence

Country-specific seroprevalence including 95% CI are depicted in Fig. 1. Seroprevalence by country and age group are shown in Fig. 2. In Table 2, we provided detailed information about seroprevalence stratified by country and age groups, and results from significance testing. We found no significant differences between males and females for measles, mumps, rubella, varicella, tetanus, polio types 1–3 and hepatitis A. Gender differences were only found for diphtheria and hepatitis B.

3.1.1. Measles

Country-specific measles seroprevalence was statistically significantly below the 95% herd immunity threshold for all countries except Eritrea. The lowest seroprevalence was observed for participants from Iran: overall 83.5% and for those aged 18–25 years (70%).

3.1.2. Mumps

Mumps seroprevalence ranged from 81% (Iraq) to 95.4% (Iran). All countries were above or equal to the immunity threshold of 93% for mumps, except for participants from Iraq. Age-specific seroprevalence was insufficient for Syrian participants aged 18–25 years and Iraqi participants older than >25 years.

3.1.3. Rubella

The overall rubella seroprevalence was above or comparable to the 95% threshold for participants from all countries, except for Iraq (84%). Stratified by age group, only three subgroups were below the threshold: those aged 18–25 from Iraq (88%, borderline significant), and those aged 26–35 years from Syria (89.4%) and Iraq (80%), respectively.

3.1.4. Varicella

Varicella seroprevalence was above the threshold of 91% for all countries and ranged from 91.7% for Iran to 98% for participants for Iraq, respectively. None of the age-group specific seroprevalences were below the threshold.

3.1.5. Diphtheria

Diphtheria seroprevalence ranged from 65% for Afghan participants to 88.1% for Iranian participants. Only the seroprevalence for participants from Afghanistan was below the established immunity threshold of 80%. Diphtheria seroprevalence was higher in men (83%) than women (75%; P = 0.037). Basic and full protection levels differed significantly between countries (p-value < 0.001). The proportion of participants with full protection was highest for Iran (62%) and lowest for Afghanistan (27%) and Iraq (28%), respectively (Fig. 3a).

3.1.6. Tetanus

The tetanus seroprevalence was high for all countries (96% to 100.0%) except for participants from Eritrea (86%). The lowest tetanus seroprevalence was observed in Eritreans aged 36–45 years (79%). Countries differed significantly regarding the level of full and basic protection (p-value < 0.001). The level of full protection

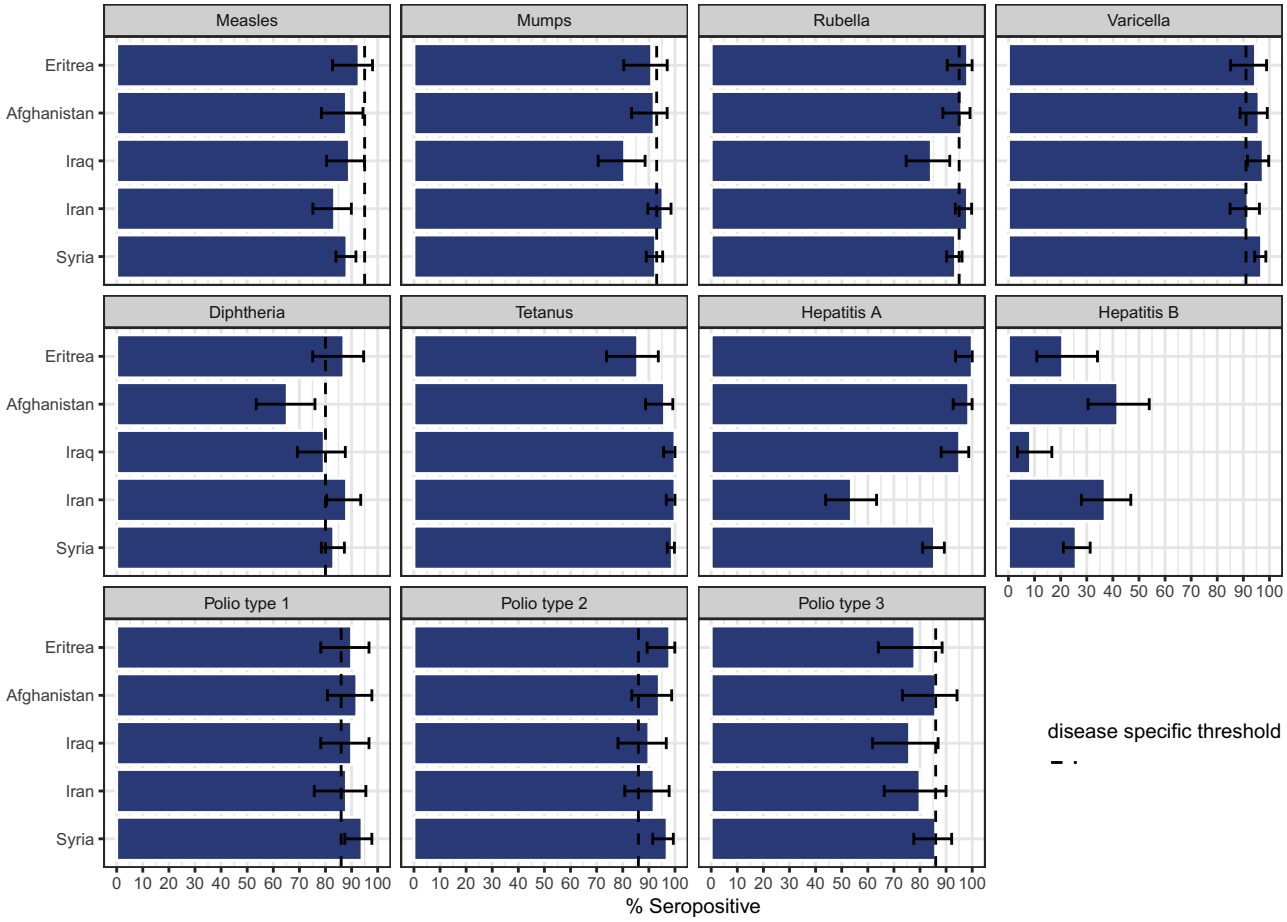

Fig. 1. Disease-specific seroprevalence including exact 95% confidence intervals by country of origin.

was highest for participants from Iran (96%) and lowest for Eritrea (41%; Fig. 3b).

3.1.7. Polio

For all three poliovirus types, seroprevalence did not differ significantly between countries, and ranged from 88 to 94% for polio type 1, 90–98% for polio type 2 and 76–86% for polio type 3, respectively. With exception of polio type 3 for Iraq (76%, P = 0.020) and – borderline – for Eritrea (78%, P = 0.052), polio seroprevalence in all other countries was not significantly below the herd immunity threshold of 86% for all polio types. Stratified by age group, only two subgroups were below the threshold: 26–35-year-olds from Iraq (63% polio type 3, P = 0.003) and Eritrea (71% polio type 3, P = 0.027).

3.1.8. Hepatitis A

Hepatitis A seroprevalence differed significantly between countries (p-value < 0.001). The seroprevalence of hepatitis A was lowest for participants from Iran (53.7%). For the other countries it ranged from 85% (Syria) to 100% (Eritrea). Hepatitis A seroprevalence significantly increased with age for participants from Syria (75% in 18–25 years to 96% in 36–45 years, p-value < 0.001) and Iran (from 42–44% in 18 to 35 years to 91% in 36–45 years, p-value = 0.001).

3.1.9. Hepatitis B

Vaccine induced immunity for hepatitis B ranged from 4.8% for participants from Iraq to 34.3% for participants from Iran. Women (29.8%) more often had vaccine induced antibody levels than men (17.7%, p = 0.004). Syrian participants aged 18–25 years, Iranians aged 18–35 years and Afghans aged 36–45 had the highest prevalence of immunity through vaccination (36–39%, Fig. 4). Markers indicating resolved or chronic infection (anti-HBc) were most often present in participants from Eritrea (25%) and least often in participants from Iran (4.6%). Anti-HBc prevalence increased with age with the exception of participants from Afghanistan, where 9 of 36 participants (25%) in the 18–25 year age group had markers indicating a natural infection. Seven participants had a chronic HBV infection (HBsAg): of these, three were from Eritrea (6%), three from Syria (1.0%), and one from Afghanistan (1%).

3.2. Self reported childhood vaccination

In total, 526/615 participants (84.6%) indicated they had received childhood vaccinations, 74 (11.9%) did not know and 15 (2.4%) indicated they were not vaccinated as a child. Measles protection was comparable between these three groups: 87.6%, 89.2% and 86.7% for 'vaccinated', 'don't know' and 'not vaccinated', respectively (P = 0.921). For tetanus, these percentages were different between the groups: 82.9%, 66.2% and 53.5% for 'vaccinated', 'don't know' and 'not vaccinated', respectively (P < 0.001).

4. Discussion

This study showed that in 2016 the overall seroprevalence for mumps, rubella, varicella, diphtheria, tetanus, polio and hepatitis A was generally high among adult asylum seekers in the Netherlands. However, measles seroprevalence was below the herd immunity threshold for all but one country of origin. Measles sero-

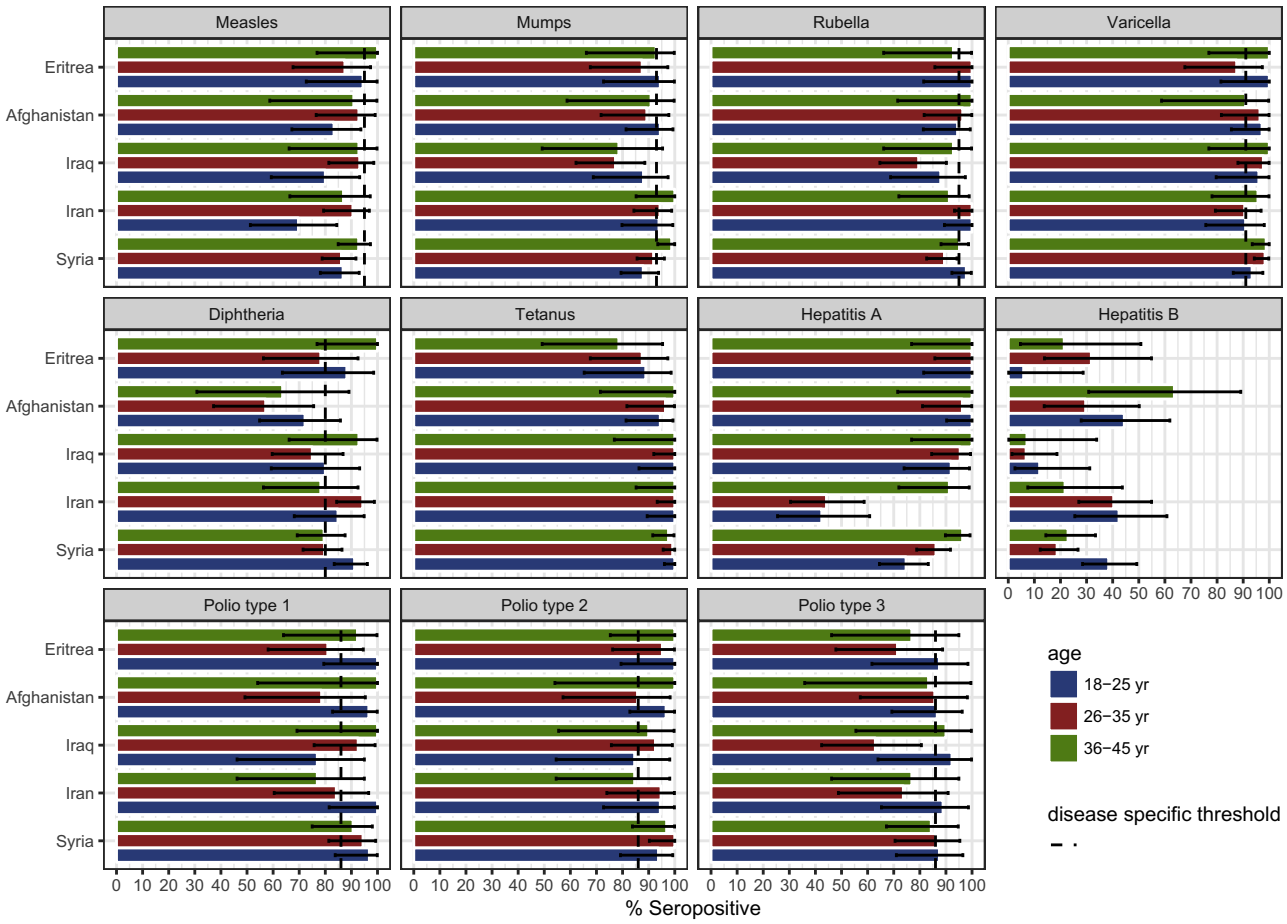

Fig. 2. Disease-specific seroprevalence including exact 95% confidence intervals by country of origin and age groups.

prevalence was lowest among adults younger than 25 years. This is likely due to suboptimal vaccination coverage combined with decreased circulation of measles virus. Our study population was born between 1970 and 1998. In the 1980s, based on data reported to the WHO, vaccination coverage for 'measles containing vaccine' was low, and ranged from ≤10% for Syria, Afghanistan and Ethiopia (which included Eritrea at the time before its independence in 1993) to ∼40% for Iran and Iraq. In the 1990s, reported measles vaccination coverage increased to 90% for Syria and 95% for Iran and Iraq, respectively, whereas coverage remained low for Afghanistan, Eritrea and Ethiopia (range: 30–40%) [19].

Our findings for measles, rubella and varicella are largely in line with those reported in recent studies from Germany [9,10]. Although age groups were not directly comparable between our study and that of Toikkanen et al. [9], both studies showed that the seroprevalence against measles was relatively low in young adults from Iran, Iraq, Syria and Afghanistan. For rubella, immunity was below the 95% threshold for 26–35 year old asylum seekers from Syria and Iraq, which was similar to findings by Toikkanen and colleagues [9]. In contrast, full immunity for diphtheria and tetanus was lower in asylum seekers tested in Germany compared to this study, with seroprevalences of 23.9% versus 38.6% for diphtheria and 43.7% versus 80.2% for tetanus, respectively [11]. In the former study, seroprevalence was not stratified by country of origin, hence it was not possible to further compare these differences.

The conclusions of our and the German studies are based on humoral immunity outcome (antibodies), however, in addition also cellular immunity contributes to immunity against infectious diseases. This implies that overall protection against vaccine preventable diseases could be under-estimated.

As the interpretation and potential implications of our findings regarding the risk of adult asylum seekers to contract VPD largely depend on the context in which adult asylum seekers reside in, as well as the level of social or geographical clustering, we discuss different contexts separately in the sections hereafter:

In **countries with high vaccination coverage,** such as The Netherlands, adult asylum seekers who are not sufficiently protected are likely to be protected by herd immunity. Levels of immunity for measles, mumps, rubella, diphtheria and polio, are high in the general Dutch population [20–23]. Refugees with a resident status are usually housed throughout the country and will therefore be geographically distributed over the country, although social clustering of susceptible refugees may occur. Even though our study shows that asylum seekers are generally adequately protected, susceptible asylum seekers can potentially be exposed to certain VPDs. For instance, varicella is not included in the Dutch NIP and is highly endemic among toddlers. The Netherlands has experienced outbreaks of measles, mumps and rubella in the past decade [24–26]. These outbreaks were largely confined to orthodox Protestants, who often refuse vaccination on religious grounds (vaccination coverage in these communities is ∼60%) and who live in socially and geographically clustered communities; the so-called 'Bible Belt' [26]. Mumps outbreaks have also occurred among students who are at risk of infection due to waning vaccine-induced immunity and social clustering [27]. We consider the risk of adult asylum seekers to contract mumps in the Netherlands to be low, as the high immunity in the asylum seeker population is likely acquired through natural infection, resulting in a stronger immune response compared to vaccination. Mumps vaccination was generally not yet included in the national immunisation programs in the

Table 2
Total number of adult asylum seekers (total n), disease-specific seroprotection levels (%) and exact 95% confidence intervals (95% CI) by country of birth and age group in years, The Netherlands, July–August 2016.

Country of birth:		Syria			Iran			Iraq			Afghanistan			Eritrea			Total n
Disease	Age group	Total n	%	95% CI	Total n	%	95% CI	Total n	%	95% CI	Total n	%	95% CI	Total n	%	95% CI	
Measles [a]	18–25	91	**87**	78–93	33	**70**	51–84	25	**80**	59–93	36	**83**	67–94	18	94	73–100	203
	26–35	123	**86.2**	78.8–91.7	53	91	79–97	44	93	81–99	28	93	77–99	24	**88**	68–97	272
	36–45	83	**93**	85–97	23	**87**	66–97	14	93	66–100	11	91	59–100	14	100	77–100[b]	145
	Total	297	**88.2**	84.0–91.7	109	**83.5**	75.1–89.9	83	**89**	80–95	75	**88**	78–94	56	93	83–98	620
Mumps [a]	18–25	91	**88**	79–94	33	94	80–99	25	88	62–89	36	94	81–99	18	94	73–100	203
	26–35	123	91.9	85.6–96.0	53	94	84–99	44	**77**	49–95	28	89	72–98	24	88	68–97	272
	36–45	83	99	94–100[b]	23	100	85–100[b]	14	**79**	49–95	11	91	59–100	14	93	66–100	145
	Total	297	92.6	89.0–95.2	109	95.4	89.6–98.5	83	**81**	71–89	75	92	83–97	56	91	80–97	620
Rubella [a]	18–25	91	98	92–100	33	100	89–100[b]	25	**88**[c]	69–98	36	94	81–99	18	100	82–100[b]	203
	26–35	123	**89.4**	82.6–94.3	53	100	93–100[b]	44	**80**	65–90	28	96	82–100	24	100	86–100[b]	272
	36–45	83	95	88–99	23	91	72–99	14	93	66–100	11	100	72–100[b]	14	93	66–100	145
	Total	297	93.6	90.2–96.1	109	98.2	93.5–99.8	83	**84**	75–91	75	96	89–99	56	98	90–100[b]	620
Varicella [a]	18–25	91	93	86–98	33	91	76–98	25	96	80–100	36	97	86–100	18	100	82–100[b]	203
	26–35	123	98.4	94.3–99.8	53	91	79–97	44	98	88–100	28	96	82–100	24	88	68–97	272
	36–45	83	99	94–100[b]	23	96	78–100	14	100	77–100[b]	11	91	59–100	14	100	77–100[b]	145
	Total	297	97.0	94.3–98.6	109	91.7	84.9–96.1	83	98	92–100	75	96	89–99	56	95	85–99	620
Diphtheria [a]	18–25	91	91	83–96	33	85	68–95	25	80	59–93	36	72	55–86	17	88	64–99	202
	26–35	123	79.7	71.5–86.4	53	94	84–99	44	75	60–87	28	**57**	37–76	23	78	56–93	271
	36–45	83	80	69–88	23	78	56–93	14	93	66–100	11	64	31–89	14	100	77–100[b]	145
	Total	297	83.2	78.4–87.2	109	88.1	80.5–93.4	83	80	69–88	75	**65**	54–76	54	87	75–95	618
Tetanus	18–25	91	100.0	96–100[b]	33	100	89–100[b]	25	100	86–100[b]	36	94	81–99	17	89	65–99	202
	26–35	123	99.2	95.6–100[b]	53	100	93–100[b]	44	100	92–100[b]	28	96	82–100	23	88	68–97	271
	36–45	83	98	92–100	23	100	85–100[b]	14	100	77–100[b]	11	100	72–100[b]	14	79	49–95	145
	Total	297	99.0	97.1–99.8	109	100	96.7–100[b]	83	100	96–100[b]	75	96	89–99	54	86	74–94	618
Polio type 1[a]	18–25	32	97	84–100	18	100	82–100[b]	13	77	46–95	30	97	83–100	16	100	79–100[b]	109
	26–35	36	94	81–99	19	84	60–97	27	93	76–99	14	79	49–95	21	81	58–95	117
	36–45	32	91	75–98	13	77	46–95	10	100	69–100[b]	6	100	54– 100[b]	13	92	64–100	74
	Total	100	94.0	87.4–97.8	50	88	76–96	50	90	78–97	50	92	81–98	50	90	78–97	300
Polio type 2[a]	18–25	32	94	79–99	18	94	73–100	13	85	55–98	30	97	83–100	16	100	79– 100[b]	109
	26–35	36	100	90–100[b]	19	95	74–100	27	93	76–99	14	86	57–98	21	95	76–100	117
	36–45	32	97	84–100	13	85	55–98	10	90	56–100	6	100	54–100[b]	13	100	75–100[b]	74
	Total	100	97.0	91.5–99.4	50	92	81–98	50	90	78–97	50	94	84–99	50	98	89–100	300
Polio type 3[a]	18–25	32	88	71–97	18	89	65–99	13	92	64–100	30	87	69–96	16	88	62–98	109
	26–35	36	86	71–95	19	74	49–91	27	**63**	42–81	14	86	57–98	21	**71**	48–89	117
	36–45	32	84	67–95	13	77	46–95	10	90	56–100	6	83	36–100	13	80	46–95	74
	Total	100	86.0	77.6–92.1	50	80	66–90	50	**76**	62–87	50	86	73–94	50	**78**[c]	64–89	300
Hepatitis A	18–25	91	75	65–83	33	42	26–61	25	92	74–99	36	100	90–100[b]	18	100	82–100[b]	203
	26–35	123	86.2	78.8–91.7	52	44	31–59	44	96	85–99	27	96	81–100	24	100	86–100[b]	270
	36–45	83	96	90–99	23	91	72–99	14	100	77–100[b]	11	100	72–100[b]	14	100	77–100[b]	145
	Total	297	85.5	81.0–89.3	108	53.7	43.8–63.3	83	95	88–99	74	99	93–100[b]	56	100	94–100[b]	618
Hepatitis B (anti-HBs)	18–25	91	39	28–49	33	42	26–61	25	12	3–31	36	44	28–62	17	6	0.1–29	202
	26–35	123	18.7	12.2–26.7	52	40	27–55	44	7	1–19	27	30	14–50	22	32	14–55	268
	36–45	83	23	14–33	23	22	8–44	14	7	0.2–34	11	64	31–89	14	21	5–51	145
	Total	297	25.9	21.0–31.3	108	37.0	28–47	83	8	4–17	74	42	31–54	53	21	11–34	615

[a] Seroprotection levels depicted in bold face indicate that the level of protection in the respective subgroup was significantly lower compared to the respective disease-specific herd immunity threshold (p-value < 0.05): Significance testing was conducted using an one-sided z-test comparing observed seroprotection levels against the herd immunity threshold of 95% for measles and rubella [17], or against the upper limits of established threshold for immunity for varicella (91%), mumps (93%), diphtheria (80%) and polio (86%), as described here [18].
[b] One-sided, 97.5% confidence interval.
[c] Borderline significant (p-value-range = 0.052–0.054).

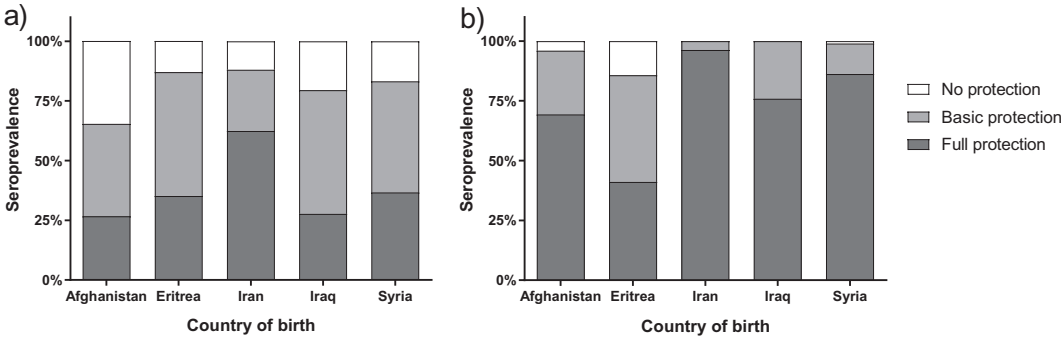

Fig. 3. Seroprevalence of (a) diphtheria and (b) tetanus stratified by basic and full seroprotection levels.

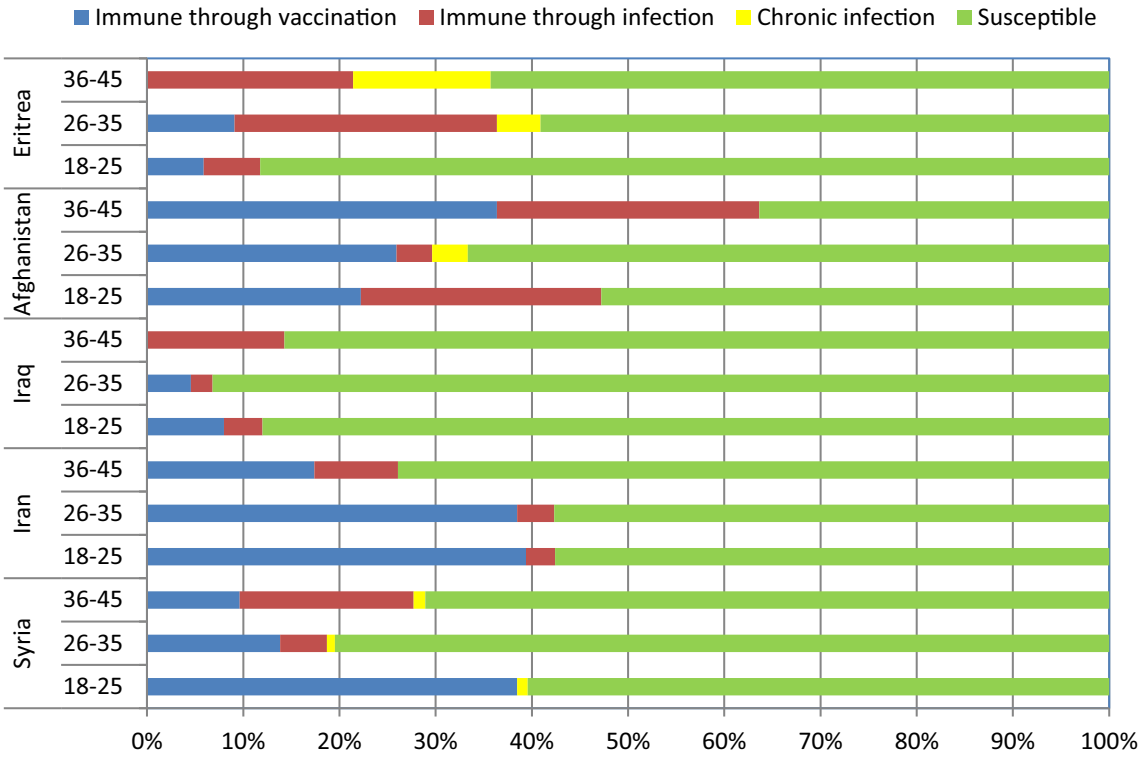

Fig. 4. Distribution of serological status for hepatitis B by county of origin and age group.

countries of origin of our study population. Diphtheria, tetanus and polio are extremely rare in the Netherlands.

In **a wider European and global context** it is important to take the epidemiological situation into account, regarding risk of exposure and susceptibility of refugees, for instance during their flight. Over the recent months, the number of measles notifications has been increasing in Europe, especially in Southern and South-Eastern Europe [28]. This means susceptible refugees could be at risk of measles exposure in parts of Europe. With regard to the global polio eradication initiative it is reassuring that the seroprevalence of antibodies against polio among adult asylum seekers was generally high in our study. However, the current outbreak of vaccine-derived polio type 2 in Syria stresses the importance of maintaining a high vaccination coverage [29]. Compared to our findings, a study among asylum seekers in the United States reported lower seroprevalences, with 80.5% for type 1, 87% for type 2 and 71.1% for type 3. Similar to our results, seroprevalence was lower against type 3 compared to types 1 and 2 [30]. An Italian study reported particularly high seroprevalence against all three polio types among mainly African asylum seekers (99.5–99.8%) [31].

Crowded asylum seeker accommodations constitute vulnerable settings for outbreaks, in particular for measles. Although measles outbreaks have not occurred in reception centres in the Netherlands, an outbreak did occur in a refugee settlement comparable to a shanty town in France in 2016, where the likely index case was identified to be a volunteer [2]. The seroprevalence for hepatitis A in the general Dutch population is 39%, with the susceptible population becoming younger [32]. Hepatitis A transmission in the Netherlands is relatively rare, although an outbreak among men who have sex with men is currently ongoing [33]. Immunity against hepatitis A is higher in asylum seekers (84%), compared to the general Dutch population, but outbreaks of hepatitis A in asylum seeker settings have been described [3,4]. Our findings can support discussions until what age hepatitis A vaccinations should be offered to asylum seekers in case of an outbreak in a reception centre. Diphtheria cases among refugees in Europe have occurred in recent years, suggesting potential occasional diphtheria transmission in refugee camp settings [6]. Our study showed that diphtheria seroprevalence was lowest among adults from Afghanistan. However, exposure in the Netherlands is unlikely, as the diphtheria seroprevalence in is high (91%) [34].

Regarding the implications of our findings for **individuals**, rubella, varicella, tetanus and hepatitis B immunity are of particular interest. Rubella and varicella immunity was high among adult asylum seekers and did not differ between sexes. Varicella vaccination is not included in the Dutch National Immunisation Programme. Whereas the mean age of infection in the Netherlands is relatively low and >95% of children are immune by the age of six [35], the risk of varicella complications increases with age and varicella infection during pregnancy or shortly after birth can cause severe disability in the new-born [36]. These consequences emphasise the importance of sufficiently high immunity levels against varicella. In the Netherlands pregnant asylum seekers are screened for rubella and varicella [37]. Given the high seroprevalence of 94% for varicella and 92% for rubella among female participants in this study, one could question the need for routine screening of pregnant women. However, exposure to varicella is likely due to high circulation in the Netherlands and, although rubella is not endemic in the Netherlands, outbreaks in the Bible Belt region occur occasionally. Furthermore, our study only included 117 women from five countries, hence representativeness and extrapolation to the wider group of pregnant asylum seekers may be limited.

Tetanus immunity was high (>90%) for most subgroups, except for study participants from Eritrea (~80%). This is similar to the Dutch population, where tetanus seroprevalence is 91%. [11]. According to WHO immunization coverage data, diphtheria and tetanus vaccination coverage has been around 20% in the 1980 s and 1990s in Afghanistan [19]. This may explain our findings regarding diphtheria, but does not align with the high tetanus seroprevalence for this subgroup. As antibodies against tetanus can only be acquired through vaccination, the high seroprevalance

in our study population suggest a higher vaccination coverage. Possibly, tetanus vaccination could have been received in adulthood, e.g. after an accident or during military service. This may also explain our finding that 53% of those who reported not to be vaccinated as a child, had tetanus immunity.

Vaccine-induced immunity against hepatitis B virus (HBV) differed by country and was 5–6% in participants from Eritrea and Iraq, and 20–34% in participants from Syria, Afghanistan and Iran. The higher prevalence of vaccine-induced immunity in women might be related to vaccination in the context of antenatal care. Overall hepatitis B immunity, including immunity through natural infection was lowest in participants from Iraq (8%) and highest in those from Afghanistan (42%). The incidence of acute HBV infection in the Netherlands is very low (0.6 per 100,000 population) [38], which points to a low risk of acquiring HBV and therefore does not indicate additional vaccination needs. However, the relatively high prevalence of chronic infection, especially among Eritreans, supports the recent recommendation of the Dutch Health Council to offer screening for chronic HBV infection to migrants from intermediate or high-endemic countries [39].

This study had several limitations. Firstly, as we only recruited asylum seekers from countries that accounted for the majority of the asylum seeker population in The Netherlands and Europe in 2015, the findings of this study cannot be extrapolated to the general adult asylum seeker population. As of June 2017, the distribution of countries of origin is similar to that of 2015 [12]. However, this might change in the future. Secondly, the subgroup analysis was performed on relatively small groups of asylum seekers, resulting in wide confidence intervals. Thirdly, the majority of participants in our study were male (81%). This can mostly be explained by the gender imbalance in reception centres in the Netherlands where the majority is male (i.e. 72% at the time of the study). However, we do not believe that the overrepresentation of men has influenced our results, as there were no differences in seroprevalence between men and women for most VPDs.

A strength of this study is that nine VPDs were investigated. As we reported serological results by country of birth and age group, our study provides detailed information on immunity against VPDs among adult asylum seekers. In particular for polio, immunity in refugees in Europe has not been recently described.

In line with previous evidence, results from our study suggest that universal vaccination of adult asylum seekers may not be necessary, considering the overall adequate levels of seroprotection in this population. However, given the immunity gaps in subgroups of adult asylum seekers for measles, offering measles vaccination to, e.g. the youngest adults (i.e. those born after 1990) could be considered, in line with ECDC and WHO which recommend to offer vaccinations according to the national vaccination program of the respective host country [1,7]. Ensuring high levels of protection against measles is of utmost importance in the progress towards elimination of measles [17], which is threatened by current outbreaks in Europe [28].

In conclusion, this study raises some concerns for measles immunity among subgroups of adult asylum seekers, especially those coming from Syria, Iran, Iraq and Afghanistan. These findings can be valuable in the context of discussions concerning vaccination and public health policies for migrants in Europe.

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Conflict of interest

None declared.

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