

1 **Seroprotection rates of vaccine-preventable diseases among newly arrived Eritrean**  
 2 **asylum seekers in Switzerland:**  
 3 **a cross-sectional study**  
 4

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## 41 **Abstract**

42 **Background** – According to 2016 WHO/UNICEF country estimates Eritrea has overall high  
43 vaccination coverage with immunisation rates for 3 doses of diphtheria/tetanus/pertussis and polio  
44 vaccine of 95%, for 2 doses measles vaccine of 85%, and for 3 doses Hepatitis B vaccine of 85%. If  
45 confirmed, this could imply that routine basic vaccination of newly arrived Eritreans could be safely  
46 omitted.

47 **Methods** – We used stored serum samples from two cross-sectional studies that screened newly  
48 arrived Eritrean refugees for infectious diseases. Consenting refugees aged 16 years and older who  
49 registered in one of three neighbouring cantons in northwestern Switzerland were enrolled between  
50 January 2016 and December 2017. Antibody titers against the following vaccine-preventable diseases  
51 were measured (applied thresholds for seroprotection in brackets): diphtheria ( $> 0.1$  IU/ml), tetanus ( $>$   
52  $0.1$  IU/ml), measles ( $> 150$  mIU/ml), rubella (only for women,  $> 11$  IU/ml), varicella ( $> 50$  mIU/ml),  
53 hepatitis B (HbsAg Index  $> 0.9$ , antiHBc Index  $> 0.9$  and antiHBs  $> 10$  IE/L). Differences between  
54 sex and age groups ( $\leq 25$  and  $>25$  years) were measured by Fisher's exact test.

55 **Results** – We analysed samples of 133 study participants (20 women, 15%) with a median age of  
56 25 years (range 16-61). Rates of sero-positivity were as follow for women / men respectively:  
57 diphtheria 57.9% / 74.8% (difference non significant), tetanus 94.8% / 41.1% ( $p < 0.001$ ), measles  
58 73.7% / 76.6% (non sig.), rubella in women 78.9%, varicella 89.5% / 95.3% (non sig.), anti-HBc  
59 15.8% / 26.2% (non sig.), and anti-HBs 15.8% / 17.8% (non sig.)

60 **Conclusion** – Sero-prevalence for vaccine-preventable infections did not meet levels required to  
61 confer herd-immunity in any of the human-to-human transmissible diseases that were studied. In  
62 general, the strategy proposed by the Federal Office of Public Health to offer basic immunization to all  
63 newly arrived refugees, including newly arriving Eritrean refugees, is justified.

64

## 65 **Key words**

66 Eritrea; asylum seekers; vaccine-preventable diseases; migrants; herd immunity; vaccination  
67 coverage

## 68 **Background**

69 In 2015 and 2016, humanitarian crises in the Middle and Far East as well as in the horn of  
70 Africa lead to a large wave of migrants seeking asylum in Europe. In most countries of origin,  
71 the public health system had seriously deteriorated, if not completely collapsed. Hence,  
72 vaccination coverage was expected to be markedly lower than in previous periods. In refugee  
73 camps the en route provision of primary health care, including immunization, relied heavily  
74 on the presence of non-governmental organisations and was impeded. Studies in newly  
75 arrived asylum seekers in Germany<sup>1-3</sup> showed seropositivity rates of various vaccine-  
76 preventable diseases (VPD) well below those known to confer herd immunity.

77 Hence, many countries receiving refugees issued blanket recommendations to offer primary  
78 immunization<sup>4-7</sup> to newly arriving refugees, irrespective of age. In Switzerland, all newly  
79 arrived asylum seekers are informed on access to screening for infectious diseases and are  
80 offered care and vaccination in federal registration centres (FRC). Recommendations to  
81 provide age-specific basic immunization to children and catch-up immunization to adults  
82 exist.<sup>8</sup> However, vaccination was explicitly delegated to primary health care physicians at the  
83 community level once the formal process of registration was finalized, i.e. often after several  
84 months. Adherence to this recommendation is not known, but likely to be low. Due to  
85 repeated outbreaks of varicella and cases of cutaneous diphtheria in asylum seekers, from  
86 2018 onward, the recommendation has changed to start a full course of age-specific basic  
87 immunization early after arrival at the FRC level.

88 Eritreans account for the largest group of asylum seekers in Switzerland<sup>9</sup> (18.7% of all newly  
89 registered asylum seekers in 2017). The Expanded Program of Immunization (EPI) in Eritrea  
90 was launched in 1980, initially including vaccines against diphtheria, pertussis, tetanus,  
91 poliomyelitis, measles and tuberculosis. However, noticeable progress in program  
92 implementation was only seen after independence in 1991. Hepatitis B was introduced in

93 2002 and the pentavalent vaccine combining the vaccines against diphtheria, pertussis,  
94 tetanus, hepatitis B and *Haemophilus influenzae* type b was introduced in 2008.  
95 According to data from the World Health Organisation and UNICEF (WHO/UNICEF),  
96 Eritrea is among one of the countries with very high vaccine coverage rates.<sup>10</sup> With reference  
97 to 2016 WHO/UNICEF data, Eritrea had a 95% coverage for the completion of three doses of  
98 diphtheria/tetanus/pertussis and polio (DTP3 and Pol3), 93% for at least one dose of a measles  
99 containing vaccine and 95% for the 3rd dose of hepatitis B containing vaccine following the  
100 birth dose. Data from an EPI coverage survey in the year 2000 among children 0-23 months  
101 showed only marginally lower coverage rates: DTP3/OPV3 coverage was 93.6%, and measles  
102 coverage (one dose) was 82.5%. These are very high coverage rates, higher than in some  
103 European countries. Consequently, young Eritrean asylum seekers may not need to be fully  
104 re-immunised upon arrival in Europe. This would save unnecessary vaccine doses at the  
105 individual as well as at public health levels. Our objective was to assess the percentage of  
106 newly arrived Eritrean asylum seekers with protective antibody titers for six VPDs. Studies on  
107 VPDs among newly arrived asylum seekers in other European countries included mainly  
108 participants from the WHO Eastern Mediterranean Region (EMRO), namely from Syria, Iran,  
109 Iraq and Afghanistan, and only few Eritreans were included. To our knowledge, this is the  
110 largest sample assessing immune responses against multiple VPDs in Eritreans.

111

## 112 **Methods**

113 We used stored serum samples from two cross-sectional studies that screened newly arrived  
114 (<12 months since entry) Eritrean asylum seekers for infectious diseases. Both studies were  
115 conducted in three neighbouring cantons in northwestern Switzerland. Recruitment and  
116 sampling methods have been published previously.<sup>11,12</sup> Samples were obtained between  
117 January 11<sup>th</sup> 2016 and December 27<sup>th</sup> 2017. Ethics approval was granted from the regional  
118 ethics committee (EKNZ 2015-353/PB\_2017-00092 Amendment 3 & 4 and EKNZ 2016-

119 00005). We enrolled consenting refugees aged  $\geq 16$  years (Cantons Basel-Stadt and -Land) or  
120 aged  $\geq 15$  (Canton Solothurn). We did not ask for vaccination history, as we could not verify  
121 this information as it is highly unlikely for this population to arrive with a vaccination card.  
122 Antibody titers against the following VPD were measured (applied thresholds for sero-  
123 protection in brackets): diphtheria ( $> 0.1$  IU/ml), tetanus ( $> 0.1$  IU/ml), measles ( $> 150$   
124 mIU/ml), rubella (only for women,  $> 11$  IU/ml), varicella ( $> 50$  mIU/ml), hepatitis B (HBsAg  
125 Index  $> 0.9$ , anti-HBc Index  $> 0.9$  and anti-HBs  $> 10$  IE/L).

#### 126 Sample preparation and analysis

127 Blood samples were collected in serum tubes and centrifuged at 2000g for 5 min after  
128 complete coagulation at room temperature. After separation, the serum was frozen in aliquots  
129 at minus 20°C until performance of serological tests. Rubella virus IgG and hepatitis B virus  
130 (HBs Antigen qualitative, anti-HBc total Ig, anti-HBs IgG were analysed on an Architect®  
131 system (Abbott, Chicago, USA), a fully automated immune-analyser based on  
132 chemiluminescent microparticle immunoassays (CMIA). IgG antibodies against measles and  
133 varicella virus were determined using Serion ELISA classic measles Virus IgG kit and  
134 varicella zoster virus IgG, respectively (Virion/Serion GmbH, Würzburg, Germany)  
135 according to the manufacturer's instruction. IgG diphtheria and IgG tetanus antibodies were  
136 detected by VaccZyme diphtheria toxoid IgG ELISA and VaccZyme tetanus toxoid IgG  
137 ELISA from Binding site (Birmingham, UK).

138 Results are presented as median titers and interquartile ranges (IQR), and percentage of the  
139 participants with a titer above the indicated threshold for sero-protection. Fisher's exact test  
140 was used to detect differences between sex and age groups ( $\leq 25$  and  $> 25$  years of age).

141 These two age groups correspond to about half of the participant population but they also  
142 represent those born before and after 1991, the year of Eritrean independence and when EPI  
143 implementation started to progress.

144 All serological analyses were performed at the Institute for Infectious Diseases, University of  
145 Bern.

## 146 **Results**

147 We included 133 Eritrean asylum seekers with a median age of 25 years (range 16-61), 47.4%  
148 were  $\leq 25$  years old, and 98.5% were below the age of 45 years. Women made up 15% (n=20)  
149 of all participants.

150 The distribution of disease-specific sero-prevalence is presented in table 1, table 2 and figure  
151 1. There was no difference in sero-protection rates between the sexes except for tetanus,  
152 where 18 (95%) out of 19 women had a positive titer compared to 44 (41%) out of 107 men  
153 ( $p < 0.001$ ). In the age group above 25 years, 36% had positive antibodies against the Hepatitis  
154 B core antigen (anti-HBc) compared to 11% in those younger than 25 years ( $p = 0.001$ ).  
155 Similarly, in the older age group 23% had antibodies against Hepatitis B surface antigen (anti-  
156 HBs) compared to 11% in the younger group (trend,  $p = 0.097$ ). In the whole population  
157 69.9% remained susceptible for Hepatitis B infection and would qualify for vaccination. For  
158 the other diseases, there was no difference between the two age groups, though point  
159 estimates indicated a trend towards higher sero-prevalence in those older than 25 years (data  
160 not shown).

## 161 **Discussion**

162 In newly arrived Eritrean asylum seekers, we found overall lower rates of sero-positivity for  
163 VPDs than anticipated - given the WHO/UNICEF immunization coverage figures for Eritrea  
164 in 2016.<sup>10</sup> Sero-prevalence in this population failed to reach the threshold expected to confer  
165 herd immunity against measles and rubella ( $\geq 95\%$ <sup>13</sup>) and against diphtheria and varicella  
166 (80% and 91% respectively<sup>14</sup>). The implications are that this population remains vulnerable to  
167 primary infection with these diseases after arrival in Switzerland.

168 Our study shows lower rates of sero-positivity for measles, rubella, and varicella than other  
169 European studies among newly arrived asylum seekers in the same period. A study from  
170 Germany reported an overall IgG sero-positivity of 88.5% for measles, 77.9% for rubella and  
171 95.9% for varicella.<sup>2</sup> However, the majority of participants in that study (83%) were from the  
172 WHO Eastern Mediterranean Region (EMRO) and only 4.6% from African regions. Another  
173 study in the Netherlands showed a relatively high overall sero-protection rate in 622  
174 participants: 88% for measles, 94% for rubella and 96% for varicella.<sup>3</sup> Again, most study  
175 participants were from EMRO, and only 9% (n=56) were from Eritrea. An Italian study<sup>15</sup>,  
176 including 134 Eritreans, found 79.9% positive measles antibodies in this population, this is  
177 closer to the rate reported in our study (76.2%).

178 Furthermore, regarding diphtheria and tetanus, the latter study found high overall sero-  
179 protection rates of 82% and 98% respectively.<sup>3</sup> Eritreans, however, were the exception, with a  
180 markedly lower tetanus sero-prevalence of 41%. Another study conducted in Germany<sup>1</sup>  
181 (without mention of country of origin of asylum seekers) found similarly low levels of sero-  
182 protection, stating that only 43.7% and 23.9% had sufficient tetanus respectively diphtheria  
183 IgG levels that corresponded to long-term protection. Our study corresponds to these results:  
184 only 68.4% of both sexes showed to have a positive titer for diphtheria and only 41.1% of  
185 men had a positive titer for tetanus. However, women showed a surprisingly high percentage  
186 with positive tetanus titers (95%), most probably indicating that they had received booster  
187 doses in pregnancies (as recommended by the WHO).

188 Nearly one quarter of the study participants showed positive Hepatitis B core antibodies (anti-  
189 HBc), as a marker of past or current infection with Hepatitis B. However, only 1.5% had a  
190 positive HBs-antigen, indicative of chronic infection. This implies that most participants had  
191 experienced functional cure with loss of HBs-antigen. This result goes in line with data from  
192 general estimates for Eritrea<sup>16</sup>, which classify it as one of only three countries in the African



193 region with a prevalence of positive HBs-antigen of < 5%. Immunity to Hepatitis B, as  
194 measured by positive Hepatitis B surface antibodies (anti-HBs), was only found in 16.5% of  
195 the participants.

196 One of the strengths of this study is that it provides data for the largest asylum seeker  
197 population in Switzerland, for whom so far data has been lacking. Furthermore, age  
198 distribution of the study population is similar to the data provided by the federal asylum  
199 seekers statistics,<sup>9</sup> allowing us to assume that our data are representative for the population of  
200 Eritrean asylum seekers.

201 The limitations of our study lie in the moderate sample size and the low number of female  
202 participants (15%). In addition, only humoral antibody response was measured, and follow-up  
203 antibody titers in response to booster doses to assess cellular memory function was not  
204 measured. Hence, boostable cellular immunity to these diseases may be underestimated.

205 In summary, we found insufficient levels of sero-protection for all measured VPDs in this  
206 population, leaving them vulnerable to primary infection within Switzerland. The  
207 recommendation to offer basic immunization to all newly arrived asylum seekers in  
208 Switzerland appears justified, also for persons originating from Eritrea.

## 209 **Conflict of interest**

210 The authors have declared no conflict of interest.

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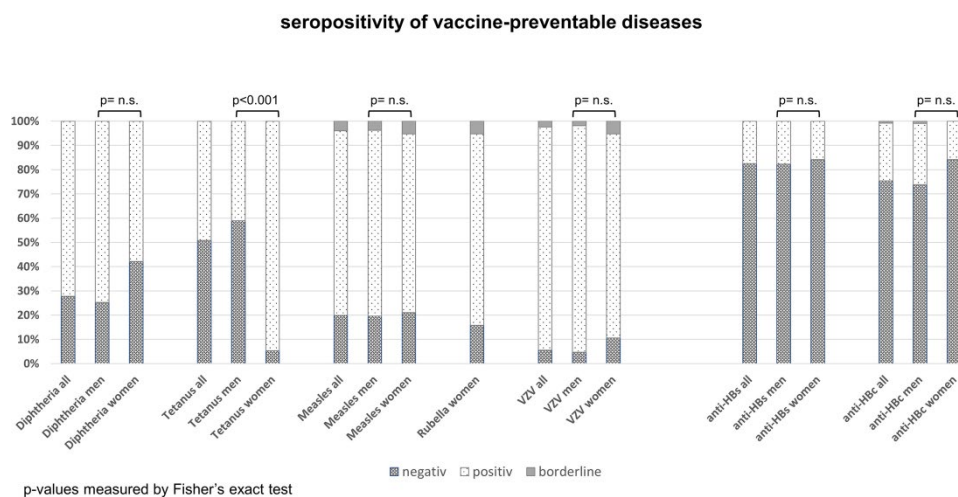
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269

270 Table 1 – Serology results of Diphtheria, Tetanus, Measles, Rubella and Varicella

	reference		median titer (IQR)	positive* % (n)	weakly positive % (n)	border line % (n)	negative % (n)	missing % (n) <sup>&amp;</sup>	p- value% men vs. women
<b>Diphtheria IgG [IU/ml]</b>	positive >0.1	all	0.17 (0.10 – 0.44)	68.4% (91)	na	na	26.3% (35)	5.3% (7)	0.17
		women		57.9% (11)			42.1% (8)		
		men		74.8% (80)			25.2% (27)		
<b>Tetanus IgG [IU/ml]</b>	positive >0.1	all	0.09 (0.07 – 0.48)	46.6% (62)	na	na	48.1% (64)	5.3% (7)	<0.01
		women		94.8% (18)			5.3% (1)		
		men		41.1% (44)			58.9% (63)		
<b>Measles IgG [mIU/ml]</b>	negative <150 borderline ≥150-200 positive >200	all	639 (205 – 1465)	76.2% (96)	na	4.0% (5)	19.8% (25)	5.3% (7)	

		women	73.7% (14)		5.3% (1)	21.0% (4)		
		men	76.6% (82)		3.7% (4)	19.6% (21)		0.8
<b>Measles IgG [mIU/ml], if borderline positive</b>	negative <150	<b>all</b>	<b>639 (205 - 1465 )</b>	<b>75.9% (101)</b>	na	na	<b>18.8% (25)</b>	5.3% (7)
	positive ≥150	women		78.9% (15)			21.0% (4)	
		men		80.4% (86)			19.6% (21)	
<b>Rubella IgG [IU/ml], only women, n=20 (15%)</b>	negative <5	women	<b>29.8 (21.6 - 73.3)</b>	<b>78.9% (15)</b>	na	<b>5.3% (1)</b>	<b>15.8% (3)</b>	5% (1)
	borderline ≥5-10 positive >10	men						n.a.
<b>VZV IgG [mIU/ml]</b>	negative <50	<b>all</b>	<b>473 (222 - 849)</b>	<b>87.2% (116)</b>	<b>2.3% (3)</b>	na	<b>5.3% (7)</b>	5.3% (7)
	weakly positive ≥50-100	women		84.2% (16)	5.3% (1)		10.5% (2)	
		positive >100	men		93.5%	1.9%		4.7%

				(100)	(2)		(5)		
<b>VZV</b>			<b>473</b>						
<b>IgG</b>		<b>all</b>	<b>(222</b>	<b>89.5%</b>			<b>5.3%</b>		
<b>[mIU/ml], if</b>	negative <50		<b>–</b>	<b>(119)</b>			<b>(7)</b>		
<b>weakly</b>	positive ≥50	wom		89.5%	na	na	10.5	5.3%	
<b>posi-</b>		en		(17)			% (2)	(7)	
<b>tive to</b>		men		95.3%			4.7%		0.28
<b>pos.</b>				(102)			(5)		

271 Abbreviations and footnotes: VZV – Varicella-Zoster virus; IU/ml – international units / millilitre; \* positive indicates the

272 percentage of participants with a titer that confers protection; & missing are always data from the same 6 men and 1

273 woman; % Fisher's exact test

274

275 **Table 2 – Hepatitis B status among Eritrean asylum seekers**

	All* <sup>&amp;</sup> , in %
<b>Susceptible</b>	69.9%
<b>Chronic Hepatitis B</b>	1.5%
<b>Immunity from previous infection</b>	21.8%
<b>Immunity from vaccination</b>	0.8%

276 \*p-value for difference between sexes (Fisher's exact) for all analyses &gt;0.5

277 <sup>&</sup> missing values: 7

278 Definitions

- 279 - Susceptible: HBs-antigen negative | anti-HBc and anti-HBs negative
- 280 - Chronic Hepatitis B: HBs-antigen positive | anti-HBc and anti-HBs negative
- 281 - Immunity from previous infection: HBs-antigen negative | anti-HBc positive +/- anti-HBs
- 282 - Immunity from vaccination: HBs-antigen and anti-HBc negative | anti-HBs positive

283