

Migration and Outbreaks of Vaccine-Preventable Disease in Europe: A Systematic Review

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Abstract

Migrant populations are one of several under-immunised groups in the EU/EEA, yet little is known about their involvement in outbreaks of vaccine-preventable diseases (VPDs). This information is vital to develop targeted strategies to improve the health of diverse migrant communities. We did a systematic review (PROSPERO CRD42019157473; January 2000 to October 2019) adhering to PRISMA guidelines, to identify studies on VPD outbreaks (measles, mumps, rubella, diphtheria, pertussis, polio, hepatitis A, *N meningitidis*, and *H influenzae*) involving migrants residing in the EU/EEA and Switzerland.

We identified 45 studies, reporting on 47 distinct VPD outbreaks across 13 countries. Most reported outbreaks involving migrants were of measles (n=24; 6578 cases), followed by varicella (n=11; 596 cases), hepatitis A (n=7; 1510 cases), rubella (n=3; 487 cases) and mumps (n=2; 295 cases). 19 (40%) outbreaks, predominantly varicella and measles, were reported in temporary refugee camps or shelters. Of 11 varicella outbreaks, 82% were associated with adult migrants. Half of measles outbreaks (n=12) were associated with migrants from Eastern European countries. In conclusion, migrants are involved in VPD outbreaks in Europe, with adult and child refugees residing in shelters or temporary camps at particular risk, alongside specific nationality groups. Vulnerability varies by disease, setting and demographics, highlighting the importance of tailoring catch-up vaccination interventions to specific groups in order to meet regional and global vaccination targets. A better understanding of vaccine access and intent in migrant groups and a greater focus on co-designing interventions is urgently needed, with direct implications for COVID-19 vaccine delivery.

Introduction

Migration to the EU/EEA and Switzerland has risen substantially in recent years and includes a diverse group of asylum seekers, refugees, labour migrants, EU/EEA internal migrants, and undocumented migrants from many regions of the world, with considerable implications for health services (1). The number of international migrants in Europe increased from around 55 million in 2000 to 82 million in 2019, with an increase of nearly 10 per cent between 2015 and 2019 (2). In 2020, 11.9% of the EU population were born outside of their country of residence, of which over 2.5 million were refugees (3). Migrants are considered to be one of several under-immunised groups in Europe (1, 4, 5). The European Vaccine Plan (6) asks Member States to pay particular attention to migrants, international travellers, and other marginalised communities to ensure their access to effective and culturally appropriate immunisation services. Some migrant groups in Europe may come from countries with limited or disrupted health and vaccination systems and may therefore be unaligned with the vaccination schedule of their host country. Certain settings, such as refugee camps and immigration detention centres, may also be extremely conducive to vaccine-preventable disease (VPD) outbreaks with unsanitary living conditions, lack of access to healthcare often combined with low vaccination coverage of residents (7).

Some migrant groups, particularly refugees, asylum seekers or undocumented migrants, may face barriers in access to health services, exclusion from services due to lack of entitlement to free health care, and inconsistencies in delivery of care, including for catch-up vaccinations and other preventative health-care services (7, 8). There are currently shortfalls in catch-up vaccination delivery for migrants on arrival to the EU/EEA, particularly among older age-groups outside routine childhood vaccination schedules. Language is often a key barrier for migrants accessing vaccination services (8) as well as a lack of systems in place for catch-up vaccination in adolescent and adult migrants (9). Some migrants, mainly those living without documentation, may also fear approaching healthcare providers, including vaccination services, because of links with immigration authorities (10). Data suggest that low confidence in vaccination could also contribute to low immunisation coverage of some migrant groups (11, 12), yet it is unclear to what extent or specific migrant groups are vaccine hesitant (13). These factors hold immediate

relevance to current COVID-19 vaccination roll-out, with some migrant groups in one study expressing specific fears or concerns around being vaccinated for COVID-19 in the UK (14).

Although migrant communities have been affected by VPD outbreaks in EU/EEA countries, the link between migration and outbreaks has been poorly elucidated to date. It is essential that further research is carried out to identify drivers and risk-factors to inform targeted strategies for improving vaccination uptake in at-risk populations. Several major measles outbreaks have been recorded in Europe in recent years, with over 60,000 cases and 98 deaths reported since January 2015 (data to September 2020), thought to involve under-vaccinated adult migrants (15, 16). Major measles clusters in Greece, Belgium and Germany during 2019 suggested that migrants from Eastern European countries may be heavily affected compared to other populations (17-19). Despite the availability of a vaccine for both, an average of almost 15,000 hepatitis A cases and 16,000 mumps cases occur across the EU/EEA each year (data from 2007-2019). An EU-wide outbreak of Hepatitis A led to a peak of 26,000 cases and 19 deaths in 2017 (16). Whilst rubella incidence in the region is generally low, with 382 cases reported in 2019 and 136 in 2020, major peaks have occurred, most recently at over 21,000 cases and one death in 2012 (16).

Regional databases do not currently collate data on VPD incidence disaggregated by migrant status, meaning the impact of VPD outbreaks on migrants is currently a poorly evidenced aspect of public health policy in Europe. What data do exist is often not disaggregated and therefore gives little information on high-risk groups, including specific nationalities. These data are vital if we are to develop effective and targeted vaccination interventions to ensure immunisation coverage reaches established Herd Immunity Threshold (HIT) targets to prevent VPD outbreaks (20, 21). Ensuring high levels of vaccination coverage is a key priority for European countries through the European Vaccine Action Plan (6), to prevent outbreaks with unnecessary morbidity, mortality and costs to health care systems.

We therefore did a systematic review to collate data from all outbreaks of key VPDs involving migrants in EU/EEA countries and Switzerland, to identify key risk factors involved.

Methods

Search strategy and selection criteria

We did a systematic literature review in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (22) and registered on PROSPERO (International prospective Register of Systematic Reviews; CRD42019157473). Primary outcomes were migrant cases of vaccine-preventable diseases as part of an outbreak; secondary outcomes were risk factors associated with having a VPD (age, nationality, migrant status, setting, immunisation status). We searched Embase, Global Health, and MEDLINE for primary research reporting on VPD outbreaks involving migrant populations in the EU/EEA and Switzerland between January 1st 2000 and May 22nd 2020, with no language restrictions. A Boolean search strategy was developed containing terms relating to migration, outbreaks of VPD and European location (see Supplementary file for full search terms). Grey literature was also searched for through websites of relevant authorities (ECDC, WHO, MSF, local health authorities) and via bibliographies of included literature. Extended information on the search strategy, R script and dataset can be found at [doi:10.24376/rd.sgul.14113451](https://doi.org/10.24376/rd.sgul.14113451).

We defined a migrant as any individual born outside of the country in which data were collected (where this information was not available, reported nationality or first language were used as a proxy for foreign-born). We included papers reporting primary data from observational studies (e.g. cross-sectional, case-control or cohort studies and outbreak or case reports), conference abstracts and systematic reviews (where they presented data not published elsewhere). Comments, editorials, literature reviews and letters were excluded. Non-English papers were included to ensure that the review is representative of outbreaks occurring across Europe. Studies were eligible for inclusion if they reported primary data on one or more outbreaks involving at least one migrant in the EU/EEA and Switzerland where migrant status was clear.

We used the WHO definition to define an outbreak: “the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. An outbreak may occur in a restricted geographical area, or may extend over several countries. It may last for a few days or weeks, or for several years. A single case of a communicable disease long absent from a population, or caused by an agent (e.g. bacterium or virus) not previously recognized in that community or area, or the emergence of a previously unknown disease, may also constitute an outbreak and should be reported and investigated”(23). Therefore, for all diseases except polio, reports of single, unlinked cases of disease were excluded. Polio has been absent from the European region since 2002 (24, 25), therefore a single case would be considered an outbreak and included. Data not disaggregated into distinct outbreaks were included in the

narrative synthesis but excluded from spatial mapping. For studies reporting on multiple outbreaks, data was extracted separately for each outbreak. Where multiple studies reported on the same outbreak, the most complete description of the outbreak was included, with multiple reports included when necessary to provide required data.

Outbreaks pertaining to the following diseases were included: diphtheria, *Haemophilus influenzae* type b (Hib), hepatitis A, measles, mumps, *N. meningitidis*, pertussis, polio and rubella. We searched for studies from the following EU/EEA countries and Switzerland: Austria, Belgium, Bulgaria, Cyprus, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, and the UK.

Exclusion criteria were studies in which data were not transparently reported for migrants or migrant status could not be identified, studies reporting on fewer than two cases of a disease (except for polio), on an expected number of cases for the area or on multiple but clearly unlinked cases. Studies reporting on cases of vaccine-derived polio as opposed to wild-type polio were also excluded.

Data screening, extraction, and synthesis

AD carried out title and abstract screening, full text screening, data extraction, and quality assessment, with all steps duplicated by an independent second reviewer (SH, RH or AB), in line with PRISMA guidelines. Where decisions could not be reached, two further reviewers (SEH, KR) arbitrated. All titles and abstracts were screened for their relevance and eligibility. Full text screening was carried out for all potentially eligible studies, and reasons for exclusion recorded.

Data were extracted on the following, where available: Time period of outbreak (year, month, duration), location (country, setting i.e. temporary camps [defined as: refugee camps, shelters, asylum residences or detainment centres] or general community, population affected (migrant status [e.g. refugee, asylum seeker, students, workers], age-group, gender, nationality, ethnicity) number of cases, migrant proportion of cases, index case, reported immune status of cases (oral vaccine history or measured antibody titres), diagnostic methods and genotyping data. Where an outbreak resulted in cases in multiple settings, the setting where the majority of cases were found was reported.

Quality assessment of the included studies was carried out independently by two reviewers using the Joanna Briggs Institute (JBI) critical appraisal tool (22). 10 points were allocated to each study, with scores of 8-10 considered high quality; 5-7 medium, 1-4 low. Studies were not excluded based on quality assessment in order to increase transparency.

Spatial mapping analysis

Using the ggplot2 package in R (version 3.6.1), the number of cases in all published outbreaks involving migrants was plotted against the GPS co-ordinates of the reported outbreak location. Where an exact location was not provided, the GPS co-ordinates of the country were used. The outbreaks were colour coded by disease type.

Results

Overview of included studies

45 studies were included, reporting 47 distinct VPD outbreaks across 13 EU/EEA countries and Switzerland (Figure 1). Twenty-one outbreaks involving migrants (45%) were reported in these countries between 2000 and 2010 and 26 (55%) were reported between 2010 and 2020, including 16 (34%) since 2015. Two reports, from Spain and Germany, did not disaggregate cases into distinct outbreaks, but presented all outbreak-related cases across a specific time period (26, 27). Measles had the highest number of reports of outbreaks involving migrants (n=24; 6496 cases), followed by varicella (n=11; 505 cases), hepatitis A (n=7; 1356 cases), rubella (n=3; 487 cases) and mumps (n = 2; 293 cases). Table 1 summarises the characteristics of all included studies. In terms of quality, 23 papers were of high quality, 16 medium and 6 low, with research not excluded on the basis of quality.

Outbreak Characteristics and Settings

In 35 (74%) included outbreaks, the index case was a migrant; of which 19 outbreaks (56%) only went on to subsequently infect migrants, and 6 (18%) only clearly reported migrant status for the index case. 19 outbreaks (40%) were reported from hosting facilities for refugees and asylum seekers (temporary camps, detention centres or mass accommodations) (18, 28-39), whereas 26 (55%) outbreaks involving migrants were reported in the general community (19, 27, 39-60). Two outbreaks were reported from other settings, including an American military base in Germany (61) and a prison (62).

Of outbreaks occurring in hosting facilities for refugees and asylum seekers (n = 19), 9 (47.4%) took place between 2015 and 2020 and four reported spread to members of the local population. During these four outbreaks, the secondary cases among the local population were mostly limited; one case of hepatitis A in a health care worker (HCW) based in an affected camp (36), three HCWs and one volunteer infected with measles during an outbreak in the Calais refugee camps (28) and the son of an asylum centre worker infected with varicella (35). However, one outbreak of measles originating in asylum seekers (146 asylum seekers affected) in Berlin spread widely among the host population, resulting in 1,344 cases overall, 345 hospitalisations and the death of a 1-year old child (39). The most frequent outbreaks occurring in camp-settings were varicella (n=9) (26, 29, 32-35, 38) and measles (n=8) (18, 26, 28, 31, 37, 39), with nearly all (75%) varicella outbreaks occurring in these settings, as shown in Figure 2.

Of outbreaks occurring in the community (n = 26), 17 (65%) reported a migrant index case. These included two small outbreaks of hepatitis A in which the index cases were internationally adopted children (43, 45), a rubella outbreak originating from a Brazilian woman living in Spain (63), a small measles outbreak with a Somali child as the index case (59) and multiple measles outbreaks with index cases from Eastern European countries, predominantly of Roma ethnicity. The most common diseases causing outbreaks in the general community were measles (n=15), hepatitis A (n=5) and rubella (n=3).

Geographical distribution of VPDs: Spatial mapping analysis

Germany (n=9) (18, 31, 34, 36, 39, 54, 58, 61, 64), Spain (n=8) (45-47, 50, 63, 65-67), Italy (n=6) (35, 38, 42, 48, 49, 60, 62) and Greece (n=5) (30, 44, 52, 53, 56, 57) were the countries that most frequently reported outbreaks involving migrants between 2000 and 2020. Two thirds (n=6) of included outbreaks in Germany affected refugee or asylum-seeking populations, mostly in temporary camps, 78% (n=7) were measles outbreaks and all but one were reported in 2010 or later. All included outbreaks in Spain took place in the general community between 2000 and 2007. In Italy, the outbreaks included were equally distributed between 2000 and 2020 and half of outbreaks were of varicella. Outbreaks reported from Greece were predominantly measles (n=3) and all but one occurred in 2010 or later.

Other countries reporting outbreaks were Austria (n=1) (64), Belgium (n=1) (19), Croatia (n=2) (55), England (n=2) (40, 68), France (n=3) (28, 29, 32), Ireland (n=2) (43, 51), Norway (n=2) (41, 59), Poland (n=3) (37) and Switzerland (n=3) (33). Some clustering of diseases by country was

observed, for example, rubella outbreaks involving migrants between 2000 and 2020 were only reported in Spain (63, 66, 67). Figure 3 highlights the case-load of VPD outbreaks (n=43) involving migrants by reported location, highlighting clustering.

Measles outbreaks in migrant populations

21 reports discussing measles outbreaks were included, reporting on 24 distinct outbreaks and one report that presented all outbreak-related cases in asylum seekers in Germany from 2004 to 2014. Seven reports originated from Germany (18, 26, 31, 39, 54, 58, 61), four from Greece (52, 53, 56, 57), three from Italy (48, 49, 60), two from Spain (47, 50) and one each from Croatia (55), France (28), Ireland (51), Norway (59) and Poland (37). Eleven measles outbreaks (45.8%) were associated with Eastern European migrants, particularly of Roma ethnicity (n = 5), including nine outbreaks with an Eastern European index case (18, 39, 48, 49, 53, 54, 60, 64, 69, 70). Eight measles outbreaks were observed in refugee camps, residences or shelters and there was a high burden in children and adolescents in all settings.

Between August 2009 and July 2011, a Europe-wide outbreak occurred, which peaked in March 2010 with 6,664 cases (16) and arose from a new strain of measles virus, D4-Hamburg, which notably led to over 24,000 cases in Bulgaria (64). Nine reports of measles outbreaks involving migrants were included from this time period (31, 51, 54-56, 58, 59, 64), of which six had a high burden in migrants from Eastern European countries, mostly of Roma ethnicity (51, 54, 56-58, 64) and four had a Bulgarian index case (54, 56-58, 64). These outbreaks were often linked to very low vaccination coverage in the affected populations. In one Greek outbreak, none of the migrant cases had a recorded measles vaccination and in an Irish outbreak, only 14% and 2% of cases had evidence of having had one and two measles vaccines, respectively (51, 56). The Greek outbreak led to 83 hospitalisations, whereas in Ireland 115 hospitalisations occurred.

Post-2015, which saw a major influx of migrants to Europe (71), four measles outbreaks involving migrants were reported, two of which took place in hosting facilities for asylum seekers and refugees (18, 28). Another took place in Greece across 2017 and 2018 and was responsible for 3150 cases, of whom the majority (80.4%) were unvaccinated, with three Romanian Roma siblings reported as the index cases (53). Over half (61.3%) of the cases were hospitalised, with complications reported in 17.1% of cases and four deaths.

Varicella in migrant populations

Ten reports discussing varicella outbreaks were included, reporting on eleven distinct outbreaks and one report that presented all outbreak-related cases in asylum seekers in Germany from 2004 to 2014. Three reports came from Italy (35, 38, 62), two from France (29, 32) and Germany (26, 34) and one each from Croatia (55), England (68) and Switzerland (33). Ten of the included varicella outbreaks (83.3%) took place in refugee camps or asylum centres, of which only one case resulted in spread to the general population; the son of an asylum centre worker was infected following an outbreak in the centre (35). Populations involved in varicella outbreaks were mainly African, Middle Eastern or South Asian, with the most frequently-reported nationalities involved being Sudanese (29, 32, 35) and Somalian (33, 34, 68) (both n=3) followed by Eritrean (29, 33) and Sri Lankan (33, 35) (both n=2). In all nine papers (81.8%), the populations most affected were adults.

Following the major influx of migration to Europe in 2015, a varicella outbreak took place in an asylum centre in Italy, infecting 41 individuals of mostly East and West African origin (38). Following this outbreak, serology testing was done in the asylum centre, showing that >20% of East and Central Africans and South Asians were susceptible. Two outbreaks affected refugee camps in the Calais area, with the first resulting in 12 cases, of whom two were hospitalised for respiratory involvement, and the second 351 cases, of whom 90% were over 15 years old and two went on to suffer from pulmonary complications (29, 32).

Hepatitis A outbreaks in migrants

Eight papers included in this review reported on 7 distinct hepatitis A outbreaks involving migrants. Two papers reported on outbreaks occurring in Germany (26, 36), two in Spain (27, 45), two in Greece (30, 44) and one each in Ireland (43) and Italy (42). A total of 1,510 cases of hepatitis A were reported as part of outbreaks involving migrants, of which 1,322 (87.5%) occurred after January 2015. In four out of six outbreaks where age was reported, the majority of affected individuals were children or adolescents (<19 years). Outbreaks affecting migrants were predominantly reported to be of sub-genotype IB, similar to strains previously isolated from samples in the Middle East, Turkey, Pakistan and East Africa (30, 36, 44), in contrast to recent European hepatitis A outbreaks in native populations, where sub-genotype IA is often prevalent (36, 72-74).

Between September 2015 and March 2016, cases rose across Germany by 45% from what is to be expected (36). This dramatic increase was due to an unusually high burden of disease in migrants; of the 699 cases, 278 (40%; median age 18 years) were in asylum seekers, 90% of which were of sub-genotype IB. In 2016 and 2017, Greece reported 188 and 30 cases, respectively, of hepatitis A of mainly sub-genotype IB in the childhood refugee population, the majority of whom were Syrian nationals (30).

Rubella outbreaks in migrants

Three rubella outbreaks involving migrants were reported, all occurring in Spain (46, 63, 66, 67). Overall, 487 cases of rubella were included, of which 277 (56.9%) were migrants. Across all outbreaks, the migrants affected were predominantly Latin American, with two affecting only this group (63, 66). Around a third of cases (151; 31.0%) were reported as being in women of child-bearing age, of whom seven were pregnant and subsequently terminated their pregnancies. In two outbreaks, all affected individuals reported being unvaccinated. In the remaining outbreak, 94.3% (n=460) did not have evidence of rubella vaccination (67).

Mumps outbreaks in migrants

Mumps outbreaks were reported on in three studies (295 cases), including two distinct outbreaks (41, 65) and one report that presented all outbreak-related cases in asylum seekers in Germany from 2004 to 2014 (26). One outbreak in Spain across 17 municipalities of Almeria (65) caused 145 infections, of which a small number (4 cases) were migrants. Another outbreak in Norway was reported as having a foreign student as the index case and went on to infect 148 individuals, resulting in seven hospitalisations and one case of meningitis (41).

Discussion

Our data highlight that migrants are an at-risk group involved in VPD outbreaks in Europe, but further work is needed to explore and assess how their risk compares to that of other groups in the population, and whether their risk factors lead to more severe clinical outcomes. We have shown a disproportionate burden of outbreaks amongst adult and child migrants living in temporary shelters or camps, alongside specific nationality groups. Measles, varicella and hepatitis A were responsible for the largest burden of VPD outbreaks (n= 42, 89.4% outbreaks) involving migrants. A large majority (n = 9, 81.8%) of included varicella outbreaks were associated with adults, whereas measles and hepatitis outbreaks affected a wide range of age-groups. Half of included measles outbreaks were associated with migrants from Eastern European countries, with several outbreaks leading to high numbers of hospitalisations, complications and deaths. Our data highlight the importance of tailoring strategies for implementing catch-up vaccination to specific at-risk groups, such as refugees and asylum seekers in shared accommodation (especially measles and varicella) and those coming from countries with low underlying coverage alongside the strengthening of routine data collection, in order to avoid outbreaks of vaccine-preventable disease.

Measles, varicella and hepatitis A outbreaks were frequently reported from hosting facilities for refugees and asylum seekers, making up almost half of all outbreaks (n= 19, 40.4%) included in this systematic review. In these outbreaks, secondary cases among the local population were mostly limited, but large numbers of migrants were often affected, for example, 351 migrants in a camp in Calais during an outbreak of varicella (32). Since the large influx of migration in 2015, temporary camps have become a new feature in Europe and the numbers of forced migrants residing in such conditions continues to increase, with Greece alone hosting almost 40,000 migrants living in temporary reception centres in 2020 (75). Many stay for extensive time periods in these settlements, which often run well beyond capacity and in suboptimal conditions, including lack of basic infrastructure and sanitation facilities (76, 77). In this review, almost half (47.4%) of outbreaks occurring in temporary settlements or camps. In most cases, migrants residing in temporary camps are not included in national vaccination systems, which could mean children miss their routine vaccinations. Poor sanitation makes these settlements highly conducive to outbreaks such as hepatitis A, which can be spread through poor sanitation (7, 44). Despite this, limited interventions exist in European countries to provide vaccination services to those living in refugee camps, with NGOs often left to fill the gap (78).

Hepatitis A outbreaks among migrants were often associated with living conditions and genetically unrelated to outbreaks in the general population, amongst whom MSM (men who have sex with men) can be considered the main risk group (44). Varicella, which we have shown often causes outbreaks amongst adults in temporary camps or detention centres, some of whom required hospitalisation, is associated with more severe outcomes in adults (79). Whilst most children born in Europe will have varicella at a young age and gain immunity, less than 60% of adults from tropical countries have immunity through a varicella episode during childhood (79, 80). Varicella is not part of routine vaccination schedules in most European countries; however, our data suggests that the impact on communities living in refugee camps justifies the implementation of organised vaccination in these settings. Provision of sanitary living conditions and appropriate healthcare in refugee camps and detention centres, alongside universal vaccination of residents for key diseases, such as measles, varicella and hepatitis A, are essential to avoid further mortality. In 2014, a measles outbreak amongst young asylum seekers spread to the wider population, causing a total of 1,344 cases and leading to 345 hospitalisations and the death of a 1-year old child (39), demonstrating the potential consequences of neglecting at-risk populations. In this outbreak, the explosion of case numbers was reportedly due to insufficient case reporting, crowded asylum accommodation and lack of systematic vaccination of contacts as well as low underlying vaccine coverage in the general population. This is in contrast to other smaller outbreaks in similar settings, where case numbers and subsequent morbidity were restricted by well-implemented selective or mass vaccination campaigns (18, 28, 31), highlighting the importance of such measures in emergency situations, as well as of maintaining high immunisation coverage across the wider population. Many shelters host migrants who have been in the host country for many years, suggesting that even if the symptomatic index case is a migrant, it is likely that the infection was acquired in the host country, reinforcing the importance of ensuring a high coverage in the general population.

A key risk-factor for outbreaks is under-immunisation in the affected populations, with affected migrant groups often having particularly low vaccine coverage. Numerous previous studies have suggested migrants are an under-immunised group; we have shown in a previous systematic review and meta-analysis that migrants represent an under-immunised population in the EU for measles, mumps, diphtheria and tetanus (81). Another review has also suggested low immunity coverage in migrants and refugees to the EU compared to the host population (4). A recent study reported that the only factor associated with increased measles incidence is low vaccine coverage, rather than migration itself; the study highlights the current low coverage of the

second vaccine dose (MCV2) in many Eastern European countries, in particular Romania (coverage of 75%), a country which also has the highest measles incidence rate in the region (46.1/100,000) (82). This reflects our findings that movement of under-immunised children from Eastern Europe, mainly of Roma ethnicity, combined with pockets of under-immunisation in host countries are a linking factor between outbreaks of measles. Roma communities are an under-immunised group in a variety of settings in Europe and face many barriers to accessing vaccination, including language, trust in health services, and concerns around vaccine safety (83-86). Whilst this systematic review only included literature on Roma described as fitting our criteria for being a migrant, many more VPD outbreaks have been reported in non-migrant Roma groups (87-89). It is important that originating from a country with known low coverage rates and belonging to a Roma community are seen as distinct risk factors, as each may require different interventions. Robust scientific messaging to address community-specific trust issues has been highlighted as a key component of COVID-19 vaccine roll-out (13, 90). It is crucial going forward that interventions are developed and tailored towards migrant communities coming from countries with known low coverage rate for key VPDs, taking into account cultural factors, to build trust and reduce disparities in access to vaccination systems (14).

Whilst our systematic review has brought to light several key at-risk populations groups for specific diseases in Europe, the scope of the results is limited by the availability and quality of the datasets that have been published. Despite including ten distinct VPDs in our search strategy, only five diseases (measles, varicella, hepatitis A, rubella and mumps) returned any reports that met our inclusion criteria. Isolated cases of diphtheria (both *C. ulcerans* and *C. diphtheriae*) and meningitidis in migrants were often reported, particularly among refugees, but did not appear to spread in European settings, perhaps due to more stringent monitoring (91-95). Due to the high outbreak-causing potential of both diseases, coordinated and rigorous monitoring and reporting going forward is essential, in order to avoid a major outbreak. Few studies compare migrant incidence or involvement in outbreaks with non-migrants, making it difficult to put these data into context and determine which groups are most vulnerable. Many outbreak reports do not adequately describe demographics of cases, therefore this review may have a bias towards outbreaks where migrants were major actors, as secondary involvement of non-nationals appears less likely to be reported. Differences in reporting systems between European countries is inhibitory to the assimilation of accurate data on at-risk groups for VPD outbreaks. It is of utmost importance that demographical data on outbreaks (including

nationality and migrant status) is collected and reported in a transparent and disaggregated manner, for example, as part of the European Surveillance System (TESSy), as this can provide insight into populations who may be at particular risk as well as health system or technological weaknesses that may leave an area or population open to future outbreaks.

Recent ECDC guidelines (96) call on EU/EEA countries to offer vaccination against measles, mumps and rubella (MMR) to all migrant children and adolescents as well as adults without immunisation records, in accordance with the immunisation schedule of the host country. Adult migrants should also be given a primary series of diphtheria, tetanus, and polio vaccines. We have also shown in this systematic review the risks associated with lack of immunity to varicella, measles and hepatitis A, particularly in refugee camps, suggesting specific guidelines should also be developed to cover these vaccinations for migrants. These data provide a clear rationale for greater emphasis to be placed on developing effective and targeted strategies to improve vaccine coverage in migrants as an at-risk group, particularly for those coming from countries with known low coverage rate and adolescent or adult migrants who will not be easily incorporated into host vaccination schedules on arrival.

This will require further research to better understand vaccine uptake and demand issues in migrant groups (including confidence, convenience and complacency) and greater focus on co-designing vaccine uptake strategies in close collaboration with affected communities, as well as commissioning of health services and offering incentives for intervention development. These findings will be of key importance during the current Covid-19 vaccine roll-out, with the IOM and others specifically calling for governments to ensure an adequate COVID-19 vaccine stock be reserved for non-nationals and forcibly displaced migrants (97).

Ensuring clinicians have access to appropriate guidelines and heightened awareness of potential under-immunisation in at-risk groups presenting is a vital next step in improving vaccine coverage and preventing outbreaks and cases of preventable VPDs going forward. A specific focus needs to be placed on catch-up vaccination for adults who may be excluded from routine immunisation schedules in their host country, with an emphasis on community engagement to ensure acceptability. It is also crucial that vaccination efforts, including mass vaccination programmes in refugee camps, where poor living conditions leave many at risk, are prioritised using NGOs or other groups who have already developed connections and trust in these settings.

Conflicts of interest

We declare that we have no conflicts of interest.

Contributions

SH had the idea for this review. AD and SH designed the protocol. AD led the searches, data extraction/analysis, with input from RH and SEH. AD and SH wrote a first draft of the paper. All authors viewed and discussed the data and contributed to the writing of the paper.

Acknowledgements

This work has been funded by the NIHR (NIHR300072). AD and SEH are funded by the MRC (MR/N013638/1). SH is funded by the NIHR (NIHR Advanced Fellowship NIHR300072) and the Academy of Medical Sciences (SBF005\1111). This work has been supported by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Infections in Travellers and Migrants (ESGITM). Kieran Rustage is funded by the Rosetrees Trust (M775). SMJ was funded by the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Immunisation at the London School of Hygiene and Tropical Medicine (LSHTM) in partnership with Public Health England (PHE). AM is supported by the NIHR Applied Research Collaboration (ARC) NW London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

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Figures and Tables

Table 1. Details of all included studies including study quality (based on JBI tool, 10-point scale: 8-10 high, 5-7 medium, 1-4 low)

Author	Number of Outbreaks	Outbreak start Year	Quality score	Disease	Country	Cases	Setting	Index case	Age groups	Migrant cases
Instituto de Salud Pública 2005 (46)	1	2005	9	Rubella	Spain	460	Community	Unstated	Majority 20-29 years	54.3% non-Spanish
Instituto de Salud Pública 2007 (47)	1	2006	9	Measles	Spain	174	Community	Unstated	47.1% aged 20-34 years	15.4% cases non-Spanish
Chaud 2017 (32)	1	2016	8	Varicella	France	351	Camp	Unstated	90% aged >15 years	All
Ciancotti 2013 (27)	multiple	2003-2012	9	Hepatitis A	Spain	152	Community	N/A	Unstated	All
Ciccullo 2018 (42)	1	2016	9	Hepatitis A	Italy	141	Community	Unstated	Adults (29-47 years)	3
Curtale 2010 (48)	1	2006	7	Measles	Italy	449	Community	Child, Romanian	Unstated	Unstated
De Valliere 2011 (33)	3	2008	7	Varicella	Switzerland	2	Camp	Unstated	27 & 30 years	All
		2008		Varicella	Switzerland	2	Camp	Unstated	19 & 24 years	All
		2007		Varicella	Switzerland	15	Camp	Adult, Eritrean	Unstated	All
Domínguez 2008 (50)	1	2006	9	Measles	Spain	381	Community	Unstated	Highest incidence in <15 months	10.2% non-Spanish
Robert Koch Institute 2010 (34)	1	2010	8	Varicella	Germany	7	Camp	Unstated	Adults	All
Filia 2006 (49)	(see Curtale)		5	(see Curtale)						
Gabutti 2003 (35)	1	2002	8	Varicella	Italy	60	Camp	Adult, Sri Lankan	Adults	All except one

Garcia 2007 (65)	1	2005	8	Mumps	Spain	145	Community	Unstated	Highest incidence in 10-14 years	2.8% foreign
Gee 2010 (51)	1	2009	4	Measles	Ireland	320	Community	Adult, Health care worker	89% <20 years	Unstated
Georgakopoulou 2006 (52)	1	2005	7	Measles	Greece	171	Community	Unstated	45% <4 years, 25% >20 years	25 belong to immigrant families
Georgakopoulou 2018 (53)	1	2017	7	Measles	Greece	3150	Community	Child, Romanian	64.5% children	10.1% foreign nationals
Gold 2010 (54)	1	2010	8	Measles	Germany	48	Community	Adult, Bulgarian	47.9% 18-36 years	10 Bulgarians
Grammens 2017 (19)	1	2016	8	Measles	Belgium	177	Community	Unstated	Majority >15 years	Unstated
Ivic Hofman 2011 (55)	2	2011	6	Measles	Croatia	10	Community	Unstated	Children	All
				Varicella	Croatia	4	Community	Unstated	Children	All
Jones 2016 (28)	1	2016	7	Measles	France	13	Camp	Adult, Refugee	Mean age 25 (range 9-46)	69.2% refugees
Kieran 2011 (43)	1	2010	3	Hepatitis A	Ireland	11	Community	Child, internationally adopted	Unstated	Unstated
Kuehne 2016 (26)	multiple	2004-2014	7	Hepatitis A	Germany	2	Camp	Unstated	Unstated	All
				Measles	Germany	82	Camp	Unstated	Unstated	All
				Mumps	Germany	2	Camp	Unstated	Unstated	All
				Varicella	Germany	91	Camp	Unstated	Unstated	All
Lampl 2019 (18)	1	2018	8	Measles	Germany	11	Camp	Child, Moldovan	Unstated	All
Lemos 2004 (66)	1	2002	8	Rubella	Spain	19	Community	Unstated	Unstated	All
Lesens 2016 (29)	1	2015	9	Varicella	France	12	Camp	Adult, Sudanese	Adults (22-32 years)	All

Mancuso 2008 (61)	1	2004	7	Measles	Germany	5	Other	Child, American	Children (8-37 months)	All
Mankertz 2011 (64)	2	2010	7	Measles	Germany	4	Camp	Bulgarian	Unstated	All Bulgarian-speaking
				Measles	Austria	6	Community	Unstated	Unstated	Unstated
Martinez-Torres 2009 (67)	(see Boletin Epi de Madrid 2005)		4	(see Boletin Epi de Madrid 2005)						
Melidou 2012 (57)	1	2010	4	Measles	Greece	126	Community	Bulgarian	78% 0-14 years	High percentage Bulgarian
Mellou 2017	1	2016	9	Hepatitis A	Greece	188	Camp	Unstated	86% <15 years	89.9% refugees
Mellou 2020 (44)	1	2017	7	Hepatitis A	Greece	294	Community	Unstated	Majority children	10.2% refugees
Michaelis 2017 (36)	1	2015	7	Hepatitis A	Germany	699	Camp	Unstated	53% <19 years, median age 18 years	40% asylum seekers
Nic Lochlainn 2016 (40)	1	2014	7	Measles	UK	10	Community	Adult, Filipino	50% <3 years, 50% 25-49 years	Unstated
Nordbo 2016 (41)	1	2015	3	Mumps	Norway	148	Community	Foreign student	Students	Unstated
Perez Sautu 2011 (45)	2	2006	3	Hepatitis A	Spain	3	Community	Child, Ethiopian	2 children, 1 adult	Unstated
				Hepatitis A	Spain	20	Community	Child, Colombia	60% adults	Unstated
Pervanidou 2010 (56)	(See Melidou)		6	(See Melidou)						
Roggendorf 2012 (69)	1	2010	8	Measles	Germany	11	Community	Adolescent, Bulgarian	Children & adolescents	Unstated
Stefanoff 2005 (37)	3	2003	6	Measles	Poland	1	Camp	Unstated	93.5% <15 years	All
				Measles	Poland	13	Camp	Unstated		All
				Measles	Poland	14	Camp	Unstated		All
Takla 2012 (31)	1	2010	9	Measles	Germany	8	Camp	Adult	Median 19 years (range 4-30)	All

Torner 2008 (63)	1	2005	7	Rubella	Spain	8	Community	Adult, Brazilian	Range 21-38 years	All
Vainio 2011 (59)	1	2011	9	Measles	Norway	10	Community	Child, Somali	90% children	80% non- Norwegian
Vairo 2017 (38)	1	2015	9	Varicella	Italy	41	Camp	Unstated	Median 26 years	Unstated
Valdarchi 2008 (62)	1	2005	10	Varicella	Italy	5	Other	Adult, Italian	Range 22-32 years	40% non- Italian
Vierucci 2010 (60)	1	2008	6	Measles	Italy	44	Community	Macedonian	All <17 years, median 6 years	77.3% non- Italian
Werber 2017 (39)	1	2014	9	Measles	Germany	1344	Camp	Child, Bosnian	Median 5 years (among asylum seekers)	10.9% asylum seekers
Zhang 2020 (68)	1	2017	8	Varicella	UK	4	Camp	Unstated	Range 22-30 years	All

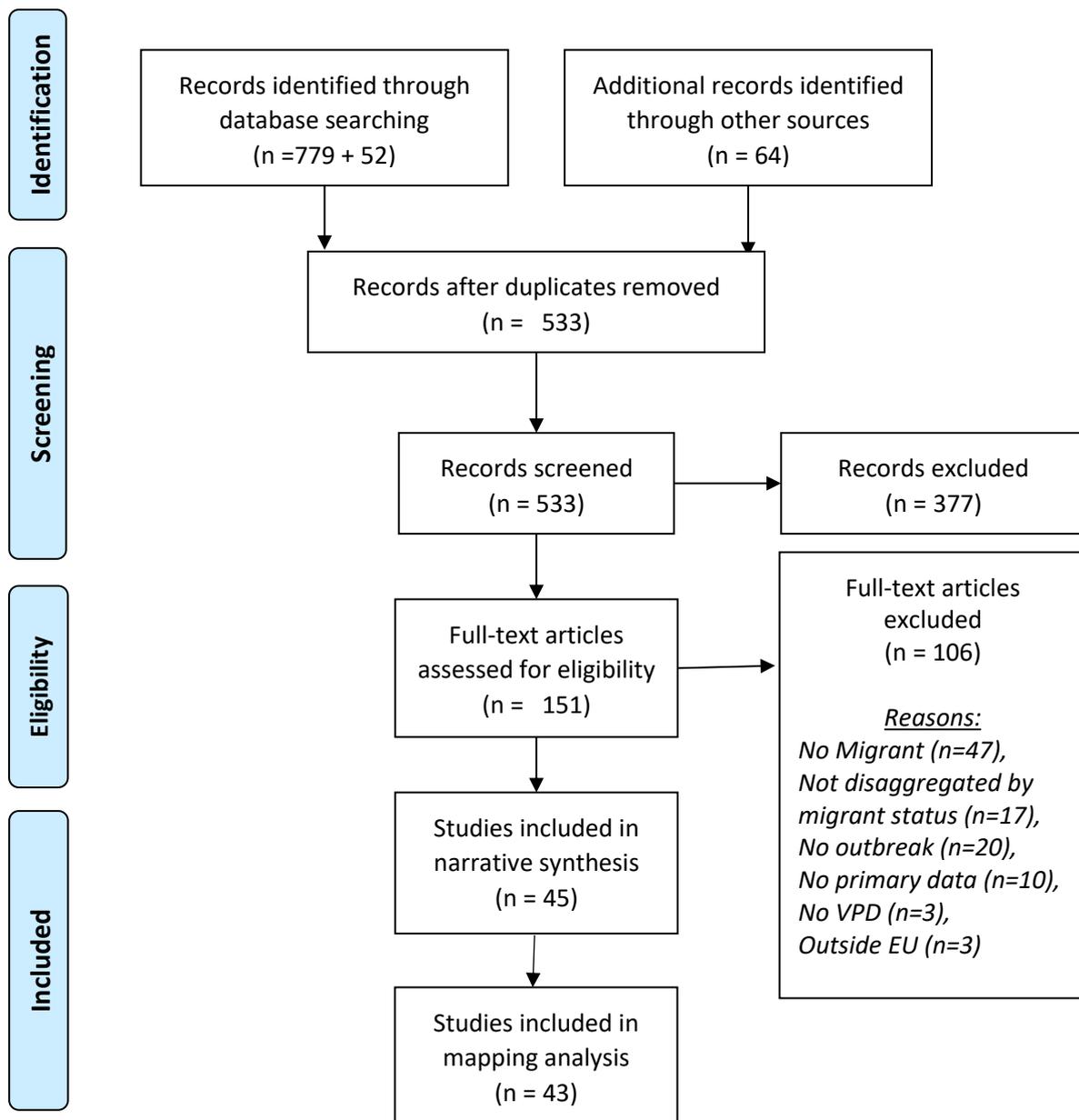


Figure 1. PRISMA diagram of included and excluded studies

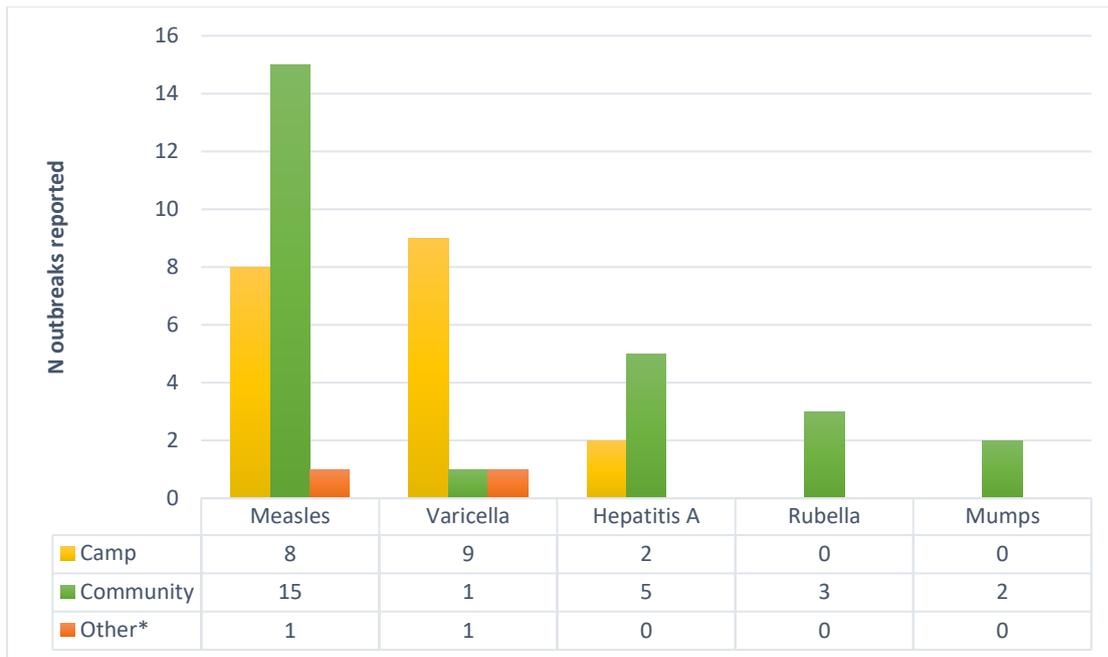


Figure 2. Settings of outbreaks involving migrants. *Other settings were a prison and a US military base.

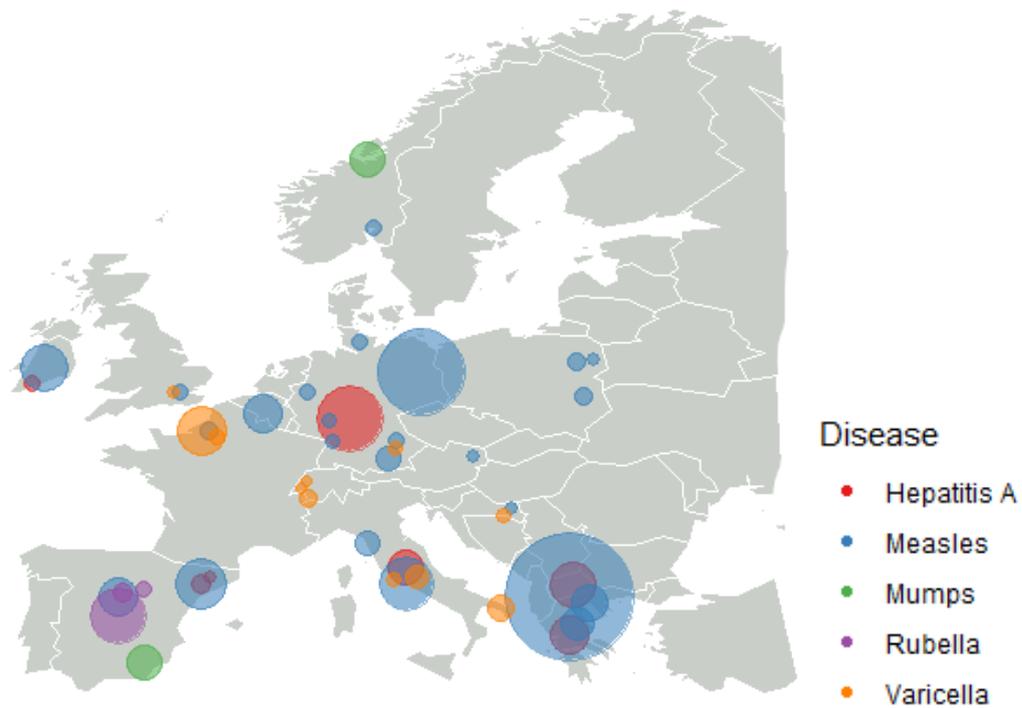


Figure 3. Case-load of vaccine-preventable disease outbreaks involving migrants by reported location. Bubble colours represent disease type, bubble size represents caseload.

Supplementary information: Key messages

Panel: Key messages

Migrants are an at-risk group involved in VPD outbreaks in Europe and comprise one of several under-immunised groups in the Region.

Adult and child migrants living in temporary shelters, camps or detention centres are at high risk from VPD outbreaks, particularly of measles, varicella and hepatitis A.

At-risk groups varied by disease; a large majority of varicella outbreaks were associated with adult migrants, whereas half of included measles outbreaks were associated with migrants of all ages from Eastern European countries, often of Roma ethnicity.

Our data highlight the importance of tailoring vaccine-delivery strategies to specific at-risk migrant groups, and strengthening routine data systems to capture data on uptake and coverage, in order to meet regional and global vaccination targets and avoid outbreaks.

Migrants may face barriers to vaccination on arrival, including exclusion from vaccination systems, with important implications for COVID-19 vaccine delivery going forward. A better understanding of vaccine uptake and demand issues in migrant groups is urgently needed, alongside a greater focus on co-designing vaccine uptake strategies in close collaboration with affected migrant communities.

Supplementary Information: Search Strategy

Search Dates: 1 st January 2000 – 22 nd May 2020	
Migrant Terms	Migrant* OR immigrat* OR emigrat* OR migrati* OR immigrant* OR emigrant* OR foreign-born* OR foreign born* OR foreign-origin OR foreign origin OR foreign* OR asylum seek* OR asylum-seek* OR refugee* OR non-citizen* OR citizenship OR nationality* OR undocumented* OR non-resident* OR transient* OR country adj3 origin* OR expat* OR newcomer* OR new-comer*
Outbreak Terms	Outbreak* OR case*
VPD Terms	Measles OR Mumps OR Rubella OR Diphtheria* OR Diphtheritic OR Pertussis OR whooping cough* OR polio* OR Hib OR Haemophilus influenza* OR Pfeiffer's bacillus OR Bacillus influenza* OR hepatitis A OR HAV OR Neisseria meningitidis OR meningococcal OR meningococemia* OR varicella OR chickenpox* or chicken pox*
EU/EEA Terms	Austria* OR Belgium OR Belgian OR Bulgaria* OR Cyprus OR Cypriot OR Czech OR Denmark OR Danish OR Estonia* OR Finland OR Finnish OR France OR French OR German* OR Greece OR Greek OR Hungary* OR Iceland* OR Ireland OR Irish OR Italy OR Italian OR Latvia* OR Liechtenstein OR Lithuania* OR Luxembourg* OR Malta OR Maltese OR Netherlands OR Dutch OR Norway OR Norwegian OR Poland OR Polish OR Portug* OR Romania* OR Slovakia* OR Slovenia* OR Spain OR Spanish OR Sweden OR Swedish OR Switzerland OR Swiss OR Great Britain OR British OR United Kingdom OR UK OR England OR English OR Wales OR Welsh OR Scotland OR Scottish OR EU OR EEA OR Europe*