RAPID RISK ASSESSMENT

# Diphtheria caused by *Corynebacterium diphtheriae* ST574 in the EU/EEA, 2025

8 July 2025

## Summary


### Epidemiological situation

Diphtheria is considered to be a rare bacterial disease in Europe. Vaccination has considerably reduced the number of cases worldwide since the 1950s, thanks to mass immunisation efforts with a safe and effective vaccine.

Following an infection, people who have not been vaccinated against diphtheria may present with skin infections (cutaneous diphtheria), classical respiratory diphtheria and in rare cases, systemic diphtheria. In highly vaccinated populations, most infections are asymptomatic or mild. Case fatality for respiratory diphtheria can be as high as 5–10%.

Between 2009 and 2020, an annual average of 21 confirmed cases of diphtheria caused by toxigenic *Corynebacterium diphtheriae* (*C. diphtheriae*) were reported across the European Union/European Economic Area (EU/EEA). In 2022, 320 cases (318 confirmed and two probable) were reported. Epidemiological investigations concluded that this increase was due to an outbreak of diphtheria caused by *C. diphtheriae*, mainly linked to migrants who had been exposed to diphtheria during migration to Europe rather than importations from countries where diphtheria remains endemic. Most cases were associated with three sequence types: ST377, ST384 and ST574.

By late 2022, rapid response measures had helped to mitigate the outbreak and the overall number of reported diphtheria cases in the EU/EEA has been steadily declining since then. However, recent data indicate that *C. diphtheriae* ST574 continued to circulate after 2022 in at least five EU/EEA countries and in Switzerland. It was noted that a significant proportion of these cases occurred in populations vulnerable to infection. Between 2023 and 2025, EU/EEA countries reported 82 cases caused by *C. diphtheriae* ST574 to ECDC. Of these, at least 25 were in individuals from vulnerable groups, including people experiencing homelessness, people who use or inject drugs, unvaccinated individuals, and older adults.

Genomic and epidemiological data available indicate local transmission in Europe among people experiencing homelessness, people who use or inject drugs, people who have not been vaccinated against diphtheria and older adults. These signals point to a wider circulation of *C. diphtheriae* ST574 across Europe. Given these findings, ECDC is making an assessment of the risk posed by *C. diphtheriae* ST574 disease acquired in the EU/EEA.

### Risk assessment

Most EU/EEA countries have very high vaccination coverage for the primary course of diphtheria-containing vaccines. In the countries with high vaccination coverage, the risk to the **general population** is assessed as **very low,** but there could be sporadic cases among groups more vulnerable to infection and pockets of unvaccinated individuals owing to possible increased circulation of *C. diphtheriae* ST574.



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The risk increases to **moderate** for **groups vulnerable to infection,** such as recently arrived migrants, people experiencing homelessness, people residing, working or volunteering in transitional housing centres, and people who use and inject drugs, if unvaccinated.

### Recommendations

- Increase awareness of diphtheria among healthcare workers, other professional caregivers, and volunteers in contact with populations more vulnerable to infection, such as recently arrived migrants, people experiencing homelessness or individuals residing, working or volunteering in transitional housing centres, and people who use or inject drugs. This includes providing information to facilitate recognition of its different forms (including cutaneous diphtheria), diagnosis and care. Furthermore, possible cases should also be isolated pending diagnostic confirmation, in accordance with national guidelines. Clinicians should be made aware of the need to consider diphtheria in the differential diagnosis of patients with a compatible clinical presentation.
- Implement health promotion activities and promote engagement with populations more vulnerable to infection. Ensure that public health measures are in place, including outbreak response, that follow ethical guidelines, safeguard individuals' rights, and minimise the risk of stigmatisation and marginalisation.
- Promote and monitor equity of access to immunisation. This particularly applies to populations more vulnerable to infection and groups at risk of being socially marginalised, such as migrants, refugees and asylum-seekers, but also disadvantaged populations (e.g. individuals living with alcohol use disorder, those who use or inject drugs, or people experiencing homelessness). Vaccination against priority diseases, such as diphtheria, poliomyelitis and measles, which are particularly prone to spreading in crowded areas, should be offered promptly, in the absence of documentation of prior vaccination. If a larger outreach is required, opportunities for broader vaccination efforts should be based on the risk profile of the group (e.g. hepatitis B).
- While prioritising immunisation to prevent disease, regularly assess the level of access to diphtheria antitoxin (DAT) and, in the context of global DAT shortages, where necessary, consider cross-border options to secure rapid access for all patients with suspected or confirmed diphtheria-toxin-induced disease.
- Conduct enhanced surveillance, including the use of molecular typing and whole genome sequencing (WGS) to confirm potential epidemiological links between cases (when relevant, and in particular in the case of potential cross-border events), to investigate the genetic determinants involved in unusual AMR patterns, and to analyse shifts in epidemiology (e.g. increases in case numbers at national or international level, involvement of atypical population groups).

# Epidemiological situation

## Event background

Diphtheria is considered to be a rare disease in Europe. Vaccination has considerably reduced the number of cases worldwide since the 1950s, thanks to mass immunisation efforts with a safe and effective vaccine. Between 2009 and 2020, an annual average of 21 confirmed cases of diphtheria caused by toxigenic *Corynebacterium diphtheriae (C. diphtheriae)* (66% male, median age: 30 years) were reported to ECDC across the EU/EEA, including UK data until 2019.

A marked shift occurred in 2022, with 318 confirmed and two probable cases of diphtheria officially reported to ECDC by EU/EEA countries (Annex, Table 1). Similar trends were also reported in other European countries (UK and Switzerland).

In response to this significant increase in case numbers an international consortium, including all affected European countries, was established to investigate the clinical, epidemiological, and microbiological aspects of this event and try to find the causes of this sudden rise. Epidemiological and microbiological investigations concluded that the increase was due to an outbreak caused by *C. diphtheriae*, mainly linked to groups of migrants who had recently arrived in Europe [1-4]. Detailed information was available for 346 cases, the vast majority of whom (98%) were young males (median age: 18 years), with ~96% having recently migrated, mostly from Afghanistan and Syria [2]. Most had travelled to EU/EEA countries using the Western Balkans route, with some using the Belarus route [1,5]. Ten European countries were affected by this outbreak, with Germany, Austria, the UK, Switzerland and France reporting the highest case numbers [2]. Clinically, the majority of cases presented as cutaneous diphtheria (77%), while 15% presented with a more severe respiratory form. The remaining cases showed less common clinical presentations. Microbiological characterisation of the outbreak isolates revealed three main sequence types (STs) involved in the outbreak: ST377, ST384, and ST574 [2]. Transmission appeared to have occurred primarily during migration or at reception centres, with no evidence of further spread to resident populations [6]. Coordinated public health measures including enhanced surveillance, targeted vaccination, prophylactic antibiotics (in some settings), case isolation, and improved hygiene and screening at reception centres all helped to mitigate the impact of the outbreak.

Since 2022, the overall number of diphtheria cases in the EU/EEA has consistently declined, with official data reported to ECDC by EU/EEA countries indicating the following trend: 165 cases in 2023, 56 cases in 2024 and 13 cases in 2025 (Annex, Table 1) [7]. However, published data and recent personal communications indicate that after the 2022 outbreak, *C. diphtheriae* ST574 continued to circulate in at least five EU/EEA countries and in Switzerland [8-13].

Austria reported to ECDC one case of *C. diphtheriae* ST574, detected in 2023 and which had an epidemiological link to a migrant/migrant facility [12].

Norway reported to ECDC one case of *C. diphtheriae* ST574, detected in 2023 in a person who had recently migrated to the country [13].

Czech public health authorities reported to ECDC eight cases of *C. diphtheriae* ST574: five in 2024 and three in 2025, suggesting ongoing circulation of ST574 in Czechia. Seven cases presented with cutaneous diphtheria, while one was a respiratory case. In terms of geographical distribution, half of the cases were detected in Prague, and the remainder were detected in other areas of the Central Bohemian region (three cases) and the South Bohemian region (one case). No data on the affected population groups are currently available [11].

In Germany a total of 126 laboratory-confirmed cases of *C. diphtheriae* ST574 have been identified across the country with 55 cases in 2022, 49 cases in 2023, 18 cases in 2024 and at least four cases in 2025 [14]. It should be noted that the reported cases have also been detected among other populations without a recent history of migration. In 2023, three cases of cutaneous diphtheria caused by *C. diphtheriae* ST574 were diagnosed in people experiencing homelessness in Frankfurt am Main, Germany. Molecular analysis linked these cases to the 2022 Europe-wide diphtheria outbreak [8]. Recently, German public health authorities reported that these cases became part of a larger cluster, comprising at least 15 cases (ST574, <9 allelic differences among them) affecting primarily but not exclusively people experiencing homelessness in the Frankfurt am Main area and individuals from other regions who had contact with people experiencing homelessness [14].

German public health authorities also reported another cluster (ST574, <8 allelic differences), including at least ten cases detected in Berlin and other federal states, spanning from January to December 2024. In terms of clinical presentation, the cases were equally split between cutaneous and respiratory presentation. All five cases involving cutaneous diphtheria were detected in Berlin in people experiencing homelessness. The respiratory cases occurred in different areas and most of them were detected among people who were not vaccinated, elderly people and/or care workers. Three deaths were reported among people with respiratory diphtheria: an unvaccinated child in Brandenburg, a nursing home resident in Saxony, and a caregiver in Lower Saxony who had travelled from Poland (Poznań area) and presumably contracted the disease there [14].

A recent publication also described a case of cutaneous diphtheria in an individual experiencing homelessness from the Poznań area, in Poland. Microbiological analyses revealed that this case was caused by *C. diphtheriae* ST574 and was genetically linked to one of the cases reported by Germany – the respiratory case in a private-care nurse who had travelled from Poland to Germany – with both isolates sharing identical allelic profiles. Although no direct epidemiological link was established, both patients lived in the same area (Poznan, a large city in western Poland). Sequencing data pointed to a common source in Poland, probably related to the 2022 outbreak, suggesting some degree of ST574 circulation in Poland in recent years [9].

In addition, in October 2023, Switzerland described three cases of diphtheria in Basel, all caused by *C. diphtheriae* ST574 [10]. Two patients presented with cutaneous diphtheria and both subsequently recovered. One of them was an individual experiencing homelessness. The third patient, an elderly woman, presented with respiratory diphtheria and died shortly after admission to hospital. All three patients were admitted to hospital within the same week, although no direct epidemiological link was identified. Molecular analyses revealed that two out of three isolates were identical and closely related (6–16 differences in single-nucleotide polymorphisms) to strains detected in asylum-seekers in Basel in 2022. ST574 was the most frequently detected ST in Switzerland during the 2022 outbreak.

These findings provide evidence of some degree of *C. diphtheriae* ST574 circulation in at least six European countries (Austria, Czechia, Germany, Norway, Poland and Switzerland) with cases involving populations more vulnerable to infection, such as people experiencing homelessness, people who use or inject drugs, unvaccinated individuals and older adults. Furthermore, Germany has reported an increase in diphtheria cases with respiratory presentation, raising concerns about more severe clinical manifestations, and possibly wider community spread [14].

# Disease characteristics

Diphtheria is a bacterial infectious disease, mostly caused by toxin-producing *C. diphtheriae* [15].The severe consequences of diphtheria can be prevented by vaccination. Humans are the only known significant reservoir for *C. diphtheriae* [16]. Transmission occurs via airborne respiratory droplets, direct contact with respiratory secretions, or indirect contact with exudate from infected cutaneous lesions or contaminated surfaces [17]. The incubation period ranges from two to five days but can be as long as 10 days [16]. Following an infection, unvaccinated individuals may present with skin infections (cutaneous diphtheria), classic respiratory diphtheria and, in rare cases, systemic diphtheria [18]. Case fatality of respiratory diphtheria can be as high as 5–10% [15].

In highly-vaccinated populations, most infections are asymptomatic or have a mild clinical course. Such cases are rarely diagnosed and reported, unless detected during active case finding or contact tracing. In symptomatic and asymptomatic infections the most common sites from which bacteria are isolated are the pharynx, larynx, tonsils, nose and skin. Other rare sites include the mucous membranes of the conjunctiva and vulvovaginal area, as well as the external auditory canal [16]. The critical diphtheria virulence factor is the production of an exotoxin (called diphtheria toxin). The gene that encodes this exotoxin (*tox*) is carried by a lysogenic prophage. The presence of the *tox* gene in a *C. diphtheriae* strain does not mean that the gene is always expressed. While non-toxigenic *tox*-gene-

bearing (NTTB) *C. diphtheriae* are rare, they are likely to be underreported in countries that do not perform phenotypic toxigenicity assays.

The World Health Organization (WHO) manual for the diagnosis of diphtheria recommends phenotypic toxigenicity assays to be performed on all samples or isolates that have tested positive for the *tox* gene [19]. The proportion of strains that carry the *tox* gene is comparatively low in the surveillance systems of high-income countries, which also screen tox-negative strains isolated serendipitously from wounds or respiratory samples. The diphtheria toxin kills tissue cells at the site of infection and produces systemic effects, including myocarditis, nephritis, polyneuropathy and paralysis, when disseminated via the bloodstream.

Non-toxigenic *C. diphtheriae* can still cause invasive infections such as endocarditis and septic arthritis, particularly in populations more vulnerable to infection [20]. Cutaneous infections with *C. diphtheriae* dominate in tropical areas and under conditions of poor hygiene and overcrowding [17,18,21]. The cutaneous lesions caused by *C. diphtheriae*, which are described as shallow greyish non-healing ulcers and can occur anywhere on the body, are often described as looking like infected insect bites. The ulcers are often co-infected with other pathogens such as *Staphylococcus aureus* and *Streptococcus pyogenes*. In high-income countries the cutaneous forms are most frequently reported among returning travellers and migrants arriving from endemic countries, individuals with waning immunity, and disadvantaged populations (e.g. individuals with alcohol use disorder, people who use drugs, and people experiencing homelessness [22–26].

Although transmission from respiratory cases via droplets is the most effective mode of infection, cutaneous carriage of *C. diphtheriae* is also an important source of person-to-person transmission, particularly in communities where vaccination coverage is low or hygiene conditions are poor. For instance, in a 1975 epidemiological study from a rural, most likely underprivileged community in the United States, transmission was shown to be higher among contacts of patients with cutaneous infections than in those with respiratory tract infections, possibly due to environmental contamination [27]. Transmission from individuals with cutaneous diphtheria may cause both respiratory and cutaneous disease in susceptible contacts [24].

The highly effective toxoid-based vaccine makes it very unusual for immunised individuals to develop the systemic toxin-mediated form of disease from cutaneous diphtheria, but they can become asymptomatic carriers of toxigenic strains and thereby facilitate spread [28,29]. Several studies highlight the role of cutaneous diphtheria infections in the spread of diphtheria and the relevance of carrier accumulation as an increased risk for an epidemic [17,24] [30,31]. The other potentially toxigenic *Corynebacteria* species, *C. ulcerans* and (very rarely) *C. pseudotuberculosis*, may also cause diphtheria disease. The vast majority of these infections are zoonotic, with human-to-human transmission almost never reported [17]. The diphtheria toxin secreted by the two species is 95% homologous to that of *C. diphtheriae* and the biological effect and clinical presentation of *C. ulcerans* and *C. pseudotuberculosis* are similar to that caused by the diphtheria toxin produced by *C. diphtheriae* [31-33].

# Microbiological information

*Corynebacterium diphtheriae* comprises several biovars (gravis, mitis, and intermedius), which are distinguished by colony morphology and biochemical properties. The gravis biovar is historically associated with more severe disease and larger outbreaks, including respiratory diphtheria with higher case-fatality rates. Mitis strains are more commonly isolated and often linked to milder or cutaneous forms, although they can also cause severe disease. Intermedius and the biovar previously known as belfanti, which is now considered a new species *C. belfantii*, are less frequently encountered; *C. belfantii* strains are typically non-toxigenic and have limited pathogenic potential.

Preliminary evidence from Germany indicates that ST574 isolates are resistant to cotrimoxazole (trimethoprim–sulfamethoxazole) [9]. A total of 105 ST574 isolates from the study by Hoefer et al. were tested biochemically, and all were found to be of biovar mitis [34].

In addition to ST574, ongoing sporadic detections of other sequence types, most notably ST377 and ST384 have been reported, raising the possibility that these lineages continue to circulate. These were the sequence types originally identified in the 2022 outbreak, which mainly affected newly-arrived migrants. It is important to note that a subset of outbreak isolates from 2022 were found to harbour key antimicrobial-resistance determinants – namely *ermX* (macrolide resistance), *pbp2m* and $bla_{\text{OXA-2}}$ (β-lactam resistance) – which, if still in the strains that are currently circulating, could compromise the effectiveness of first-line treatment options.

Recent data reported by Germany confirm the emergence of non-toxigenic *tox* gene-bearing (NTTB) variants within ST574, which carry the *tox* gene but do not express functional diphtheria toxin. These characteristics underscore the importance of integrating genomic and phenotypic surveillance to monitor both virulence and resistance trends within this evolving outbreak lineage.

The detection of isolates with higher allelic differences, novel antimicrobial resistance profiles, and the emergence of NTTB variants within the ST574 lineage collectively suggest undetected circulation of *C. diphtheriae*. The genetic diversification and evolving resistance patterns further highlight the dynamic nature of the outbreak, and reinforce the need for sustained, coordinated genomic surveillance and public health response to identify and contain emerging transmission chains.

# Diphtheria epidemiology in the EU/EEA

Diphtheria caused by *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* is a notifiable disease in the EU and countries are expected to report new cases to ECDC through EpiPulse Cases on a monthly basis, in accordance with the 2018 EU case definition for communicable diseases and ECDC reporting surveillance guidelines [35]. ECDC publishes monthly and annual reports on diphtheria [36,37].

In an outbreak situation, data from regular monthly reporting is complemented with information through other channels, such as EpiPulse Events or epidemic intelligence sources.

The EU case definition distinguishes the pathogen (*C. diphtheriae*, *C. ulcerans* or *C. pseudotuberculosis*) for the purpose of official reporting and requires isolation of toxin-producing bacteria from a clinical specimen for laboratory confirmation.

Diphtheria cases in the EU/EEA due to *C. diphtheriae* have been reported to ECDC since 2009 through TESSy/EpiPulse Cases. During the period 2022–2025, and as of 4 June 2025, 554 cases had been reported (550 confirmed, four probable) – see Table 1 showing reported cases by year and country. Cases have been reported in Germany (292), France (70), Austria (65), Belgium (43), Netherlands (23), Czechia (14), Norway (14), Slovakia (10), Latvia (7), Italy (5), Slovenia (4), Spain (3), Sweden (3) and Luxembourg (1).

Of the 554 cases reported in the period 2022–2025, 497 (90%) were among males. Cases were reported among all age groups, with a preponderance among those aged 15–24 years (58%).

Of the 554 cases, 73% (n=404) presented with an exclusively cutaneous form of the disease. A total of 62 cases had a respiratory presentation and six of these had both respiratory and cutaneous presentations. The proportion of cases with respiratory disease was 12% in 2022 (n=38), 8% (n=13) in 2023, 16% (n=9) in 2024 and 15% (n=2) in 2025. Six cases had other clinical presentations, and one case had a nasal presentation. Information on clinical presentation was missing for 81 cases.

Of the 554 cases, importation status was available for 407 cases (73%). Of these, 238 cases (58%) were imported (n=233) or import-related (n=5), 102 cases (25%) were locally acquired, and for 67 (16%) case importation status was unknown. An imported case is defined as not having resided in the country of notification during the incubation period.

Of the 554 cases, vaccination status was available for 223 cases (40%). Eighty-nine cases (40%) were not vaccinated and 31% (n=70) were vaccinated with an unknown number of doses. Sixty-four cases (29%) were reported to have been vaccinated with a known number of doses: 46 (21%) having received one dose, three (1%) having received two doses, five (2%) having received three doses, four (2%) having received four doses, five (2%) having received five doses and one (0.5%) having received six doses.

Between 2022 and 2025, 11 deaths were reported by Germany (3), France (2), Latvia (2), Austria (1), Belgium (1), Czechia (1) and Slovakia (1). Most of the deaths (n=8) resulted from respiratory diphtheria, one death had other clinical presentation and for two deaths the clinical presentation was not available. Four of the 11 fatal cases were in individuals who were unvaccinated, and vaccination status was not available for the other seven fatal cases. Sequence type was available for one death reported in 2022 (ST574).

Before 2022, during the period 2009–2021, 11 deaths were reported by Latvia (6), Belgium (1), France (1), Greece (1), Spain (1), and the United Kingdom (1). The majority of the people who died (n=8) presented with a respiratory form of the disease, two people had a respiratory and a cutaneous form of the disease and for one person details of the clinical presentation were not available. Among those who died during 2009 and 2021, six people were unvaccinated, one was vaccinated with three doses of the diphtheria vaccine and for the other four vaccination status was not available.

Following the increase in diphtheria cases in 2022, ECDC updated its reporting mechanisms for routine indicator-based surveillance and introduced new metadata for diphtheria, including variables to identify if a case is part of an outbreak or a cluster, information on whole genome sequencing and information on antibiotic susceptibility testing.

Between 2022 and 2025, information on cluster-relatedness was available in EpiPulse Cases for 101 cases. Twenty-three cases (23%) were reported as being related to a cluster, while 78 cases (77%) were not related to a cluster. Of these, cluster setting (setting where a cluster-related case has been identified) was available for 12 cases; six cases were related to a cluster which included individuals at a migrant centre, five cases were related to a family cluster and one case was related to an 'other' cluster. Of the 12 cases with information on cluster setting, sequence type was available for two cases (ST377, ST916). Detailed information on cluster setting whole genome sequencing (WGS) and antibiotic susceptibility testing results cannot be described due to limited reporting of these variables. Therefore, this information is now captured via other sources, such as Epipulse Events and other official reports.

# Diphtheria vaccination

Universal immunisation is the only effective method of preventing the toxin-mediated disease. The occurrence of diphtheria in fully vaccinated individuals is very rare. The vaccine effectively protects against the effects of the exotoxin produced by *C. diphtheriae* and *C. ulcerans*, but vaccinated individuals can still be infected by the bacteria, become asymptomatic carriers of toxin-producing strains and transmit these to others. Untreated individuals are colonised for an average of 18.5 days and 95% clear *C. diphtheriae* within an average of 48 days [29].

All EU/EEA countries have diphtheria vaccination programmes, which include a primary series and booster doses provided through childhood and adolescence [18]. The primary series, as well as the first booster, consists of a full dose of diphtheria-toxoid (D) as part of a combined vaccine (often part of the hexavalent vaccine, combining diphtheria and tetanus toxoids, acellular pertussis (DTaP) adsorbed, inactivated poliovirus (IPV), Haemophilus influenzae type b (Hib) conjugate, and hepatitis B (HepB) (recombinant) vaccine), with few exceptions. Depending on the age at the time of the booster being administered, the vaccine may contain a full dose (D) or a reduced dose (d) of diphtheria toxoid.

Booster doses in adulthood are recommended in 19 EU/EEA countries [38], with different frequencies across countries (20, 15 or 10 years), with two additional countries offering diphtheria vaccination as part of the maternal programme against pertussis. In some cases, a higher frequency of administration is recommended in older adult individuals (65 years and above).

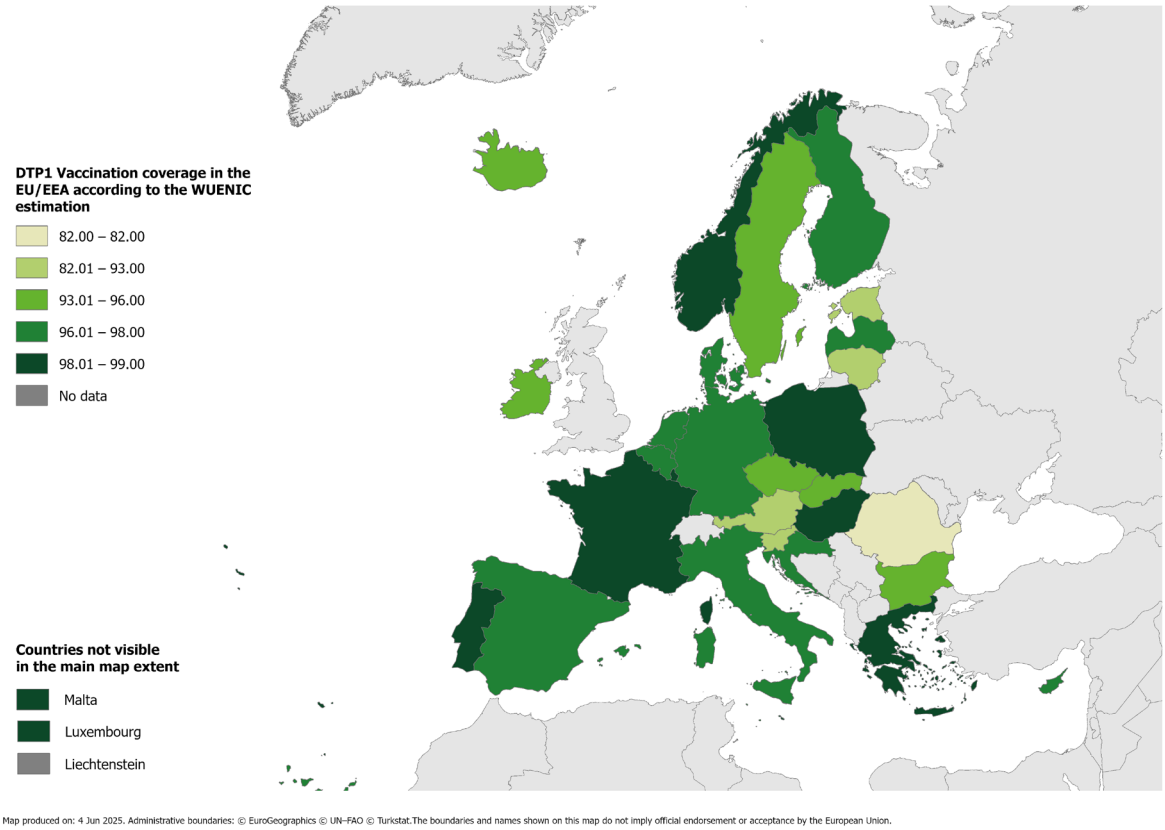
It should be noted that vaccine-induced immunity wanes with time and does not provide life-long protection. A seroprevalence study conducted with sera collected during 2015-18 in 18 European countries showed insufficient seroprotection (range of not protective level: 22.8%-82%) against diphtheria in individuals aged 40–59 years [39], underscoring the relevance of diphtheria toxoid containing booster doses in adulthood.

# Diphtheria vaccination coverage in the EU/EEA

In the EU/EEA, most countries have a high vaccine coverage for both the first dose (DTP1) and the third dose of diphtheria, tetanus toxoid and pertussis vaccine (DTP3) [40]. As shown in Figure 1 and 2 below, in 2023, DTP1 vaccine coverage ranged from 82% in Romania to 99% in France, Greece, Hungary, Luxembourg, Malta, Norway, Poland and Portugal. For the same period, DTP3 vaccine coverage ranged from 78% in Romania to 99% in Greece, Hungary, Luxembourg, and Portugal. Available data on the coverage of the fourth dose (DTP4) are limited, however, an ad-hoc data call by ECDC in 2024 showed a DTP4 vaccine coverage between 16% and 100% (median of 89.7%) for 2023 in the EU/EEA (data available for 16 countries) [41].

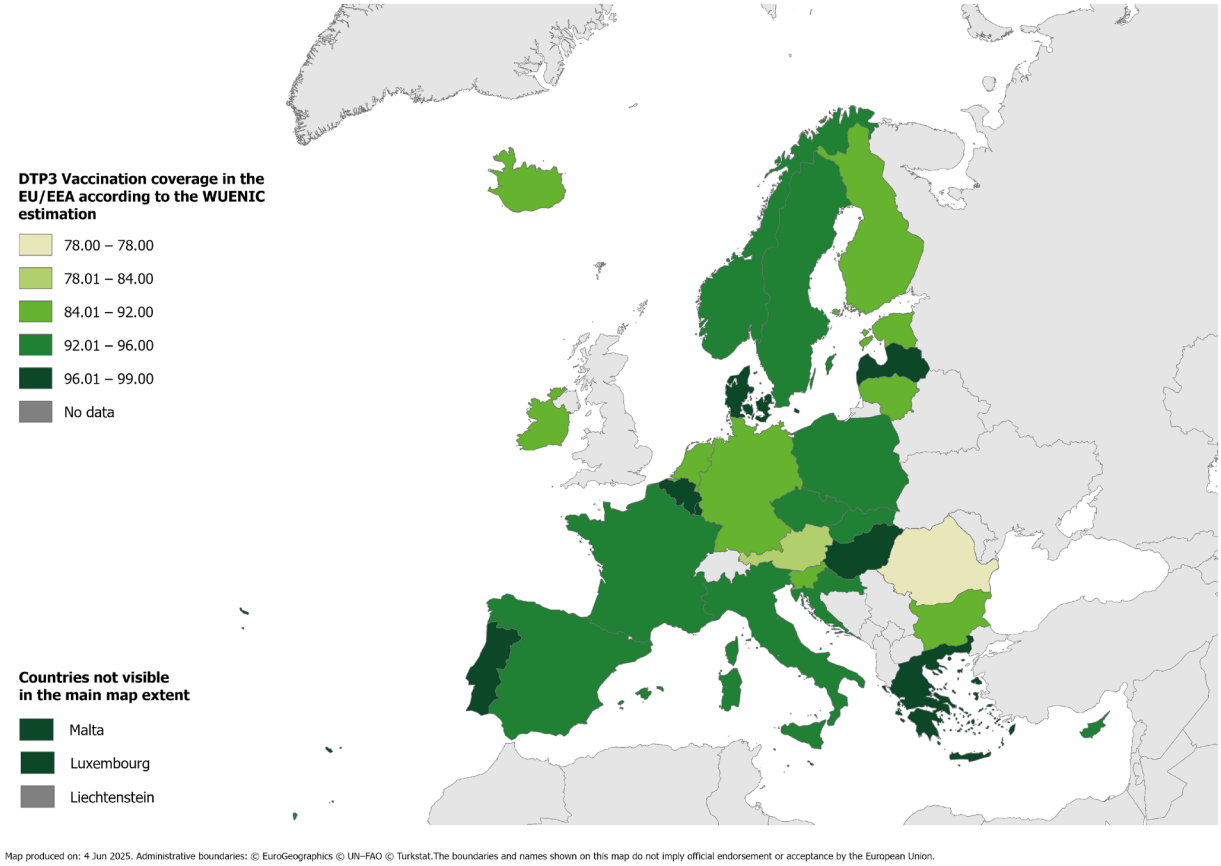
Comparing the DTP3 vaccine coverage between 2019 and 2023 showed that in 2023, 17 countries reported a decrease in vaccine coverage, with the largest declines observed in Romania (-11%), Slovenia (-6%), Ireland (-5%), and Sweden (-4%). Only Belgium showed an increase (+1%), while 11 countries reported no overall change (see Annex, Table 2).

**Figure 1. DTP1 vaccine coverage in the EU/EEA, 2023**




*Source of data: WHO Immunization Data Portal, WHO and UNICEF Estimates of National Immunization Coverage (WUENIC).*

**Figure 2. DTP3 vaccine coverage in the EU/EEA, 2023**




*Source of data: WHO Immunization Data Portal, WHO and UNICEF Estimates of National Immunization Coverage (WUENIC).*

# Diagnostics of diphtheria

Diagnostic tests used to confirm diphtheria include molecular detection and the isolation of *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* by culture and toxigenicity testing. Clinical suspicion of cutaneous diphtheria depends on epidemiological circumstances and morphological characteristics of the wound. Skin infections may be manifested by a scaling rash or ulcers with clearly demarcated edges and membrane, but any chronic skin lesion may harbour corynebacteria along with other pathogens.

There are no commercial tests available for the diagnosis of diphtheria. Laboratory identification and confirmation of diphtheria may require isolation of *C. diphtheriae*, *C. ulcerans* and *C. pseudotuberculosis* by culture from a clinical specimen (nasal swabs, pharyngeal swabs or swabs from pseudo-membrane, wound or skin lesions) and toxigenicity testing. Direct and real-time polymerase chain reaction (PCR) assays can detect the *C. diphtheriae tox* gene within a few hours, but confirmation of diphtheria toxin expression is only possible with the Elek test [42-44]. Procedures for the collection of specimens are available in WHO's Manual for laboratory diagnosis of diphtheria [42]. According to WHO guidelines, *tox* gene positive samples should be treated as probable cases and sent for phenotypic toxigenicity confirmation and further biotyping to the WHO Collaborating Centres for Diphtheria in the UK or Germany if these assays cannot be performed nationally.

Case detection is strongly influenced by the availability of laboratory resources (techniques, methods, reagents and the quality of these reagents) and technical expertise. A reliable, sensitive and prompt diphtheria laboratory service is necessary for the timely diagnosis and treatment of infections, as well as to demonstrate the absence of diphtheria transmission in the population.

The results of the External Quality Assessment (EQA) exercise carried out in 2013 in EU/EEA Member States indicate that several EU/EEA laboratories face challenges in providing quality diagnostic methods for diphtheria and sourcing reagents for the tests [44]. More recently, a WHO EQA was undertaken with a similar outcome [46]. Limitations in the capacity to confirm toxigenic infections may delay diagnosis, treatment and public health interventions in some EU Member States. Enhanced surveillance, molecular typing and WGS of patient isolates have the potential to improve the understanding and monitoring of diphtheria transmission patterns.

In May 2025, the European Commission has designated nine European Union Reference Laboratories (EURLs) for public health and among these is a reference laboratory for diphtheria and pertussis [47]. The EURLs have been set up to operate for seven years and their activities are funded under the EU4Health programme. The aim of these EURLs is to support national reference laboratories in promoting good practice and alignment by Member States on a voluntary basis with regard to diagnostics, testing methods, use of certain tests for uniform surveillance, notification and reporting of serious cross-border health threats [47].

The EU Reference Laboratory for Public Health on Diphtheria and Pertussis (EURL-PH-DIPE), a consortium led by the University of Turku, is one of the laboratories that has recently been set up and it will conduct gap analysis, perform EQAs and be available to provide guidance if necessary (eudipe@utu.fi) [48].

# Treatment of diphtheria

The rapid administration of equine diphtheria antitoxin (DAT), according to national or local guidelines, is required for the successful treatment of classic respiratory diphtheria, in combination with antibiotic treatment, and may also be required for other forms of diphtheria in rare cases. Diphtheria toxin that has already entered the host cells is unaffected by DAT. Therefore, to reduce complications and mortality, DAT should be administered as soon as possible after disease onset, preferably intravenously in serious cases [18]. As DAT neutralises circulating toxin but not bound toxin, it stops the progression of disease but does not reverse symptoms. In patients with suspected or confirmed diphtheria, WHO recommends not to perform routine sensitivity testing prior to administration of DAT [49].

The entire therapeutic dose should be administered at once. In patients with suspected or confirmed symptomatic diphtheria, WHO suggests administering a single dose of diphtheria antitoxin with the choice of dose being based on disease severity and time since symptom onset, rather than a fixed dose for all patients [49]. The dose is the same for children and adults [18]. Administration of DAT can cause acute and delayed hypersensitivity reactions. DAT treatment initiated later than 48 hours after the onset of systemic toxic symptoms has a limited impact on the clinical outcome although, if necessary, DAT can be offered at any stage of the disease [50]. DAT is included in the World Health Organization Essential Medicines List [51].

According to WHO, treatment with DAT is of limited value in cutaneous disease. In most cutaneous infections, large-scale toxin absorption is unlikely. Therefore, the risk of giving an antitoxin is usually considered substantially greater than any benefit. Nevertheless, if the cutaneous ulcer is sufficiently large (more than 2 cm squared) and membranous, then DAT may be justified [42]. In addition to antibiotic therapy surgical debridement can also help treat cutaneous diphtheria [50].

In addition to the DAT treatment, antibiotic treatment is also necessary to eliminate the bacteria and prevent further spread to susceptible individuals. Countries should follow national guidelines on case management. Most guidelines recommend treatment with a macrolide (erythromycin, azithromycin or clarithromycin), benzylpenicillin (penicillin G) or phenoxymethylpenicillin (penicillin V) for a period of 14 days. Individuals who continue to harbour the bacteria after treatment should receive an additional course of oral erythromycin and submit a new sample for culture after completion of the course.

Antibiotic resistance seems rare but strains with intermediate susceptibility to penicillin G and erythromycin have been increasingly reported in recent years [52-54]. Some respiratory diphtheria cases are particularly severe and may need tracheotomy, mechanical removal of the pseudo-membranes, intubation and ventilation (including extracorporeal membrane oxygenation (ECMO)). Patients should also be monitored for cardiac complications.

Delays in appropriate treatment with DAT and antibiotics are often the result of late clinical suspicion of disease because the treating physician may not have seen cases of diphtheria before. Detailed clinical case reports, including visual material from the outbreak observed in Europe in 2022, have been published [2].

Furthermore, patients should receive immunisation with diphtheria toxoid upon recovery since natural diphtheria infection may not confer long-standing protective immunity.

# Availability of DAT in EU/EEA Member States

Following the significant decline in incidence of diphtheria after the introduction in the 1950s of mass vaccination in Europe, the production, supply and availability of DAT to treat diphtheria infection had significantly declined in Europe and globally.

After the increase in the number of cases observed in 2022, the European Commission's Health Emergency Preparedness and Response Authority (DG HERA) signed a framework contract for the supply of DAT with Scandinavian Biopharma on 2 August 2024. This contract, negotiated on behalf of EU Member States is valid for 24 + 6 months. Eight EU Member States (Belgium, Estonia, Greece, Finland, Croatia, Malta, Romania and Slovenia) are participating. The product is manufactured by Premium Serum and Vaccines India. All imported batches are tested for potency by the National Institute for Biological Standards and Control (NIBSC) in the UK. The maximum amount of units (vials) of DAT that the contractor can supply under this framework contract is 1 600 vials.

This framework contract provides a significant opportunity to increase access and availability of DAT in EU Member States. DAT, which is in short supply across the globe, remains an essential tool for treating diphtheria.

# ECDC risk assessment for the EU/EEA

This assessment is based on evidence available to ECDC at the time of publication. It follows the ECDC rapid risk assessment methodology, where the overall risk is determined by a combination of the probability of infection and the impact of the disease on affected populations. ECDC will continue to monitor the event and reassess the risk depending on the disease trajectory and the response measures implemented.

## What is the risk associated with transmission of diphtheria ST574 in the EU/EEA?

The diphtheria cases observed among newly-arrived migrant populations since 2022 have mostly been caused by *C. diphtheriae* ST574 and transmissions occurred primarily during migration or at reception centres. During 2024 and 2025, clusters of *C. diphtheriae* ST574 occurred among other population groups, including people experiencing homelessness, people who use or inject drugs, unvaccinated individuals, and older adults, indicating autochthonous transmission. ECDC is assessing the risk posed by *C. diphtheriae* ST574 infections acquired in the EU/EEA.

## Risk for the general population

### *General population with high vaccination coverage*

High immunisation coverage in the community reduces the risk of infection and, to an even greater extent, the risk of disease in the general population. Therefore, the probability of infection among the general population with high vaccination coverage is considered **very low**. The impact of the current epidemiological situation is also expected to be **very low** for this population. Nevertheless, sporadic cases and small clusters in the community may occur due to possible pockets of unvaccinated individuals, and because circulation of *C. diphtheriae* – including that of *C. diphtheriae* ST574 – is possible even in populations with high vaccination coverage, and in the absence of detected clinical disease. Furthermore, even in countries with high coverage for the primary vaccination course, there could be significant parts of the adult and older population who have not received the recommended boosters, or who have waning immunity.

However, given the very low probability of infection and the very low impact described above, the risk assessed for the general population with high vaccination coverage in the EU/EEA is considered **very low.**

### *General population with low vaccination coverage*

The probability of infection among the general population with low vaccination coverage is considered **low** (even though there is a higher percentage of susceptible individuals compared to the population with high vaccination coverage, where the probability is very low). Circulation of *C. diphtheriae* ST574 is possible in this setting and more likely than in populations with high vaccination coverage. The public health impact of the current epidemiological situation for this population is expected to be **low** (although it is higher than for the population with high vaccination coverage, where the impact is very low, since the disease may be more severe in those not fully vaccinated).

Given the low probability of infection and the low impact described above, the risk to a general population with low vaccination coverage in the EU/EEA is still considered **low.**

## Risk for specific populations and settings

### *Vulnerable populations, such as recently arrived migrants, people experiencing homelessness or individuals residing, working or volunteering in transitional housing centres, who are fully vaccinated*

The probability that populations more vulnerable to infection, such as recently arrived migrants, people experiencing homelessness or individuals residing, working or volunteering in transitional housing centres who are fully vaccinated, may be infected by the pathogen is considered **low**. The impact of the disease in this specific population and setting with a complete diphtheria vaccination course is considered as **very low**.

Given the low probability of infection and the very low impact, the risk is considered to be **low** for fully-vaccinated individuals in these vulnerable settings.

### *Vulnerable populations, such as recently arrived migrants, people experiencing homelessness or individuals residing, working or volunteering in transitional housing centres, who are not fully vaccinated*

The probability that populations more vulnerable to infection, such as recently arrived migrants, people experiencing homelessness or individuals residing, working or volunteering in transitional housing centres who are not fully vaccinated, may be infected by the pathogen is considered **moderate**. Among these populations that are more vulnerable to infection, it is possible that exposed, unvaccinated individuals may be subject to a severe outcome following a diphtheria infection, so the impact of an outbreak in this setting would be more serious than in the broader population, for several reasons. Vulnerable populations such as migrants and people experiencing homelessness may face barriers to healthcare access and are often affected by structural determinants that may delay diagnosis and increase the impact of disease, including insufficient access to vaccination, unfavourable social, economic and living conditions, such as limited access to facilities, poor hygiene conditions and inadequate nutrition. Under circumstances where response measures are delayed due to chemoprophylaxis and DAT not being readily available, the impact may be exacerbated. The impact of the disease in this specific population and setting, involving vulnerable individuals without a complete diphtheria vaccine course, is therefore considered to be **low to moderate**.

Given the moderate probability of infection and the low-to-moderate impact, the risk is considered as **moderate** for populations more vulnerable to infection, such as people experiencing homelessness and individuals residing, working or volunteering in transitional housing centres without a complete diphtheria vaccine course.

# ECDC recommendations

**Specifically for the current event**, with clusters among populations more vulnerable to infection, such as recently arrived migrants, people experiencing homelessness, people using or injecting drugs, or individuals residing, working or volunteering in transitional housing centres, ECDC recommends that public health authorities should:

- Implement health promotion activities and promote engagement with populations more vulnerable to infection, ensure that public health measures, including outbreak response, follow ethical guidelines, safeguard individuals' rights, and minimise the risk of stigmatisation and marginalisation.
- Increase awareness of diphtheria among health care workers, other professional caregivers, and volunteers in contact with populations more vulnerable to infection, as described above. This includes providing information to facilitate recognition of its different forms (including cutaneous diphtheria), diagnosis, and care and isolating possible cases pending diagnostic confirmation, in accordance with national guidelines. Clinicians should be made aware of the need to consider diphtheria in the differential diagnosis of patients with a compatible clinical presentation.
- In the current epidemiological situation, should a new diphtheria case occur, including in vulnerable individuals who have access/links to specific settings where transmission may have been more likely, it is crucial to identify close contacts of confirmed or possible cases, monitor the clinical condition of contacts regularly for seven to 10 days, and test them (nasal, nasopharyngeal or throat swabs), irrespective of their immunisation status. Antimicrobial post-exposure prophylaxis should be provided, along with vaccination of incompletely vaccinated or unvaccinated close contacts after swabs have been collected, irrespective of cultures result and in accordance with national or regional recommendations.
- Promote and monitor equity of access to immunisation. This particularly applies to populations more vulnerable to infection or groups at risk of being socially marginalised, such as migrants, refugees and asylum-seekers, but also disadvantaged populations (e.g. individuals living with alcohol use disorder, people who use or inject drugs, or people experiencing homelessness). Vaccination against priority diseases such as diphtheria, poliomyelitis and measles, which are particularly prone to spread in crowded areas, should be offered promptly, in the absence of documentation of prior vaccination [54]. In the event of a larger outreach, broader vaccination efforts should be considered based on the risk profile of the group (e.g. hepatitis B).
- It is important to ensure the provision of booster vaccination doses for the adult and elderly population. Booster doses of diphtheria should be considered when more than 10 years have passed since the last vaccination, in line with national recommendations. Checking immunisation status during key healthcare encounters and vaccinating, when necessary, could be an effective mechanism to better integrate immunisation efforts into healthcare delivery services and promote optimal uptake.
- Conduct enhanced surveillance, including the use of molecular typing and whole genome sequencing (WGS) to confirm potential epidemiological links between cases (when relevant, and in particular in the case of potential cross-border events), to investigate the genetic determinants involved in unusual AMR patterns, and to analyse shifts in epidemiology (e.g. increases in case numbers at national or international level, involvement of atypical population groups). While this strategy involves additional resource requirements, selecting representative isolates for sequencing will mitigate the financial impact while providing all necessary characterisation data. ECDC can offer WGS support for Member States seeking assistance (microbiology@ecdc.europa.eu).
- Ensure timely notification and reporting to competent national and international authorities of cases confirmed according to the EU case definition. When reporting, complete all required fields as these data are essential for guiding recommendations and understanding transmission patterns. Investigations should aim to assess case history and other risk factors.

The EU Health Task Force (EU HTF) is available to provide support in any stage of the response to an event, either remotely or on site. Competent authorities in EU/EEA countries (ECDC national coordinators and National Focal Points) can request EUHTF support through EpiPulse or by emailing the EUHTF Coordination Team at euhtf@ecdc.europa.eu.

Furthermore, ECDC encourages EU/EEA public health authorities to focus on the activities set out below, which should be part of their routine efforts.

## Immunisation programmes

Universal immunisation with diphtheria toxoid-containing vaccine remains the only effective preventive measure for diphtheria and for controlling its spread and impact. To achieve the highest levels of protection and maximise opportunities for the prevention of diphtheria disease, public health authorities in EU/EEA countries are encouraged to consider the key actions below.

- Strengthen the implementation of routine immunisation programmes, seeking to achieve high vaccination coverage rates with the primary series of three doses of the diphtheria toxoid-containing vaccine, followed by booster doses. To ensure adequate personal protection from diphtheria, immunisation programmes should provide three primary doses and three booster doses of diphtheria-toxoid-containing vaccine, with age-appropriate formulations in terms of potency.

- Traveller vaccination is also critical. Countries should continue to advise travellers to diphtheria-endemic countries to check whether they have completed their primary vaccination series against diphtheria two weeks before departure, and to receive a booster dose of diphtheria toxoid in line with national recommendations.
- Implement systems, including the use of immunisation information systems, to identify and reach out to the unvaccinated or partially vaccinated population with a primary immunisation series and/or booster doses.
- While prioritising immunisation to prevent disease, the level of access to DAT should be regularly assessed. Given the global DAT shortages, if necessary, cross-border options could be considered in order to secure rapid access for all patients with suspected or confirmed diphtheria-toxin-induced disease.
- Develop and roll out training programmes for those providing vaccination services in order for them to be fully equipped with the relevant knowledge when faced with questions and concerns from parents. Similarly, develop and roll out targeted and tailored programmes for vaccine recipients to better understand why they are offered vaccination. Families and individuals who are not vaccinated or are hesitant about vaccination tend to cluster geographically, creating pockets of unvaccinated communities within otherwise highly vaccinated populations. This increases the risk of developing the disease if *C. diphtheriae* is introduced into these communities. ECDC has developed specific material for frontline healthcare workers, with an e-learning course to support them in their conversations on vaccination with service users [56]. A factsheet on diphtheria is available in all EU languages in the European Vaccination Information Portal [57].

### Surveillance and case management

- Apply standard and respiratory precautions when caring for confirmed or possible cases with respiratory diphtheria, and standard and contact precautions when caring for confirmed or possible cases of cutaneous diphtheria. Clinical management of confirmed cases, including the use of DAT, should be undertaken in accordance with national guidelines and WHO guidelines [49]. It should be noted that although treatment is available, timely clinical detection is important to reduce disease severity and complications [49].
- Avoid further spread and facilitate the isolation, with appropriate support, of confirmed respiratory or cutaneous cases, until the elimination of the pathogen is demonstrated by two negative cultures obtained at least 24 hours apart after completion of antimicrobial treatment.
- Ensure that proper surveillance, including adequate laboratory diagnostic capacity, is in place in each country, with clear protocols for sampling, specimen transport and testing. Prompt toxigenicity testing where needed via the EU Public Health Reference Laboratory for Diphtheria and Pertussis (EURL-PH-DIPE, (eudipe@utu.fi) or the two WHO Collaborating Centres for Diphtheria in the UK or Germany, and arrange antimicrobial susceptibility testing for timely diagnosis and appropriate treatment.
- Responsible authorities should ensure detailed documentation of the infection setting and, wherever possible, conduct an in-depth investigation of clusters to enhance insight into disease spread and conditions.

### Outreach to populations more likely to be exposed to *C. diphtheriae*

It is essential to take critical measures that help to safeguard individuals' rights, build trust, and minimise the risk of harm or stigmatisation, especially for those people who may already face barriers due to migration status, language, or fear of legal consequences. Taking these efforts into account is vital to achieving meaningful participation in testing, offering care and vaccination in a safe environment and ensuring accurate public health outcomes.

This *C. diphtheriae* ST574 event involving populations more vulnerable to infection also highlights the broader need for sustained awareness and to monitor other priority pathogens affecting people in often precarious situations, such as newly arrived migrants, those experiencing homelessness or those using or injecting drugs. These groups are at elevated risk of communicable diseases due to factors such as overcrowding, poor access to hygiene and sanitation and healthcare and incomplete vaccination coverage. Culturally sensitive and community-focused surveillance strategies targeting populations more vulnerable to infection are crucial to reduce transmission risks, address health disparities, and build trust with affected populations. These strategies should include pathogens such as *Mycobacterium tuberculosis*, *Bordetella pertussis,* hepatitis viruses, and respiratory viruses such as influenza and SARS-CoV-2.

# Limitations

This assessment was undertaken based on information known to ECDC at the time of publication. Case definition and classification used by non-EU/EEA countries may differ from the EU case definition used for diphtheria. There may be a potential under-ascertainment and/or under-reporting of diphtheria in Europe.

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# Annex

**Table 1.** ***C. diphtheriae*** **cases reported to ECDC (Tessy/EpiPulse Cases) by reporting country, 2022–2025**

| Country | 2022 | 2023 | 2024 | 2025 |
|---|---|---|---|---|
| Austria | 61** | 3 | 0 | 1 |
| Belgium | 26 | 9 | 6 | 2 |
| Czechia | 3 | 2 | 8 | 1 |
| France | 52 | 18 | 0 | 0 |
| Germany | 150 | 104** | 31 | 7 |
| Italy | 3 | 2 | 0 | 0 |
| Luxembourg | 0 | 1 | 0 | 0 |
| Latvia | 0 | 2 | 4 | 1 |
| Netherlands | 6** | 13 | 3 | 1 |
| Norway | 8 | 2 | 4 | 0 |
| Spain* | 1 | 1 | 1 | 0 |
| Sweden | 2 | 1 | 0 | 0 |
| Slovenia | 0 | 4 | 0 | 0 |
| Slovakia | 8 | 2** | 0 | 0 |
| Total | 320* | 165* | 56 | 13 |

**Cases as reported by Spain on 25 June 2025 by personal communication [58]*
***Case count includes one probable case.*

**Table 2. Diphtheria tetanus toxoid and pertussis-containing vaccine (DTP3) vaccine coverage (%) in the EU/EEA 2019–2023**

| Country | 2019 | 2020 | 2021 | 2022 | 2023 | % change* (2019–2023) |
|---|---|---|---|---|---|---|
| Austria | 85 | 85 | 86 | 84 | 84 | -1% |
| Belgium | 97 | 97 | 98 | 98 | 98 | **+1%** |
| Bulgaria | 93 | 91 | 89 | 91 | 92 | -1% |
| Croatia | 94 | 94 | 92 | 92 | 93 | -1% |
| Cyprus | 95 | 95 | 95 | 95 | 95 | **0%** |
| Czechia | 97 | 97 | 94 | 94 | 94 | -3% |
| Denmark | 97 | 97 | 97 | 97 | 97 | **0%** |
| Estonia | 91 | 91 | 90 | 90 | 90 | -1% |
| Finland | 91 | 90 | 89 | 91 | 91 | **0%** |
| France | 96 | 96 | 96 | 96 | 96 | **0%** |
| Germany | 91 | 91 | 91 | 91 | 91 | **0%** |
| Greece | 99 | 99 | 99 | 99 | 99 | **0%** |
| Hungary | 99 | 99 | 99 | 99 | 99 | **0%** |
| Iceland | 92 | 93 | 92 | 92 | 92 | **0%** |
| Ireland | 94 | 94 | 94 | 93 | 89 | -5% |
| Italy | 96 | 94 | 94 | 95 | 95 | -1% |
| Latvia | 99 | 99 | 94 | 95 | 98 | -1% |
| Lichtenstein | NDR | NDR | NDR | NDR | NDR | **NRC** |
| Lithuania | 92 | 91 | 90 | 90 | 90 | -2% |
| Luxembourg | 99 | 99 | 99 | 99 | 99 | **0%** |
| Malta | 98 | 98 | 99 | 98 | 98 | **0%** |
| Netherlands | 94 | 94 | 95 | 93 | 92 | -2% |
| Norway | 97 | 97 | 97 | 97 | 96 | -1% |
| Poland | 95 | 94 | 94 | 94 | 94 | -1% |
| Portugal | 99 | 99 | 99 | 99 | 99 | **0%** |
| Romania | 88 | 87 | 86 | 85 | 78 | -11% |
| Slovakia | 97 | 97 | 97 | 97 | 96 | -1% |
| Slovenia | 95 | 95 | 86 | 89 | 89 | -6% |
| Spain** | 95 | 94 | 92 | 93 | 93 | - |
| Sweden | 98 | 97 | 98 | 94 | 94 | -4% |
| EU/EEA | 95 | 94 | 94 | 95 | 95 | **NRC** |

*Source of data: WHO Immunization Data Portal, WHO and UNICEF Estimates of National Immunization Coverage (WUENIC).*
*NDR: no data reported*
*NRC: no rate calculated.*
** The percentage of change was calculated for each dose as the percentage of increase or decrease between 2019 and 2023 –i.e. ((coverage in 2023-coverage in 2019)/coverage in 2019) x 100.*
*** Updated data from Spain show a vaccine coverage of 93% in 2021, 95% in 2022 and 96% in 2023 published by the Ministry of Health [58,59].*