UK Health Security Agency

Public health operational guidance for Shiga toxin-producing Escherichia coli (STEC)

Including STEC O157 and non-O157 infections

January 2023

Contents

Document information

Title	Public Health Operational Guidelines for Shiga toxin-producing *Escherichia coli* (STEC)
Endorsed by	UKHSA Gastrointestinal Infections Leads Network
Approved by	Trish Mannes

Document history

Date	Reason for change	Issue number
14 June 2018	Updated guidance	STEC v1
13 July 2018	Updated leaflets	STEC v1
05 May 2022	Updated guidance	STEC v2
1 September 2022	Updated guidance	STEC v3.1

Document review plan

Responsibility for Review	UKHSA Gastrointestinal Infections Leads Network
Next review date	2027

Contact information

Name	Sooria Balasegaram
Email	Sooria.Balasegaram@phe.gov.uk

Glossary

Term	Definition
APHA	Animal and Plant Health Agency
Children aged 5 years old and under	All children up their sixth birthday
DEFRA	Department for Environment, Food and Rural Affairs
Diagnostic laboratory	Local hospital or regional laboratory services
DNA	Deoxyribonucleic acid
E. coli	*Escherichia coli*
eae	*E. coli* attachment and effacing gene
EAEC	Enteroaggregative *E. coli*
EH	Environmental Health
EHO	Environmental Health Officer
FES	Field Epidemiology Service
FSA	Food Standards Agency
FWE	Food, Water and Environmental laboratories
GBRU	Gastrointestinal Bacteria Reference Unit
GDW2	Gastro Data Warehouse (version 2)
GI	Gastrointestinal
GP	General Practitioner
HPT	Health Protection Team
HSE	Health and Safety Executive
HUS	Haemolytic Uraemic Syndrome
HUSEC	STEC strains that have been frequently reported to cause HUS
IMT	Incident management team
NHS	National Health Service
NIS	UK Health Security Agency National Infection Service
OCT	Outbreak control team
PCR	Polymerase chain reaction
PHE	Public Health England
Reference laboratory	Reference services as provided by the GBRU
RMP	Registered medical practitioner

Term	Definition
STEC	Shiga toxin-producing *Escherichia coli*
stx	Shiga toxin
SGSS	Second Generation Surveillance System
UKHSA	United Kingdom Health Security Agency
VTEC	Vero cytotoxin-producing *Escherichia coli*
WGS	Whole genome sequencing

Definitions used in this guidance

Term	Definition
aggR	The *aggR* gene encodes a protein known as the aggregative regulator (AggR) that co-ordinates the transcription of multiple virulence factors involved in adherence to the human gut mucosa. This factor is normally found in enteroaggregative *E. coli* (EAEC) but can sometimes be found in STEC (for example, an outbreak of HUS in Germany in 2011 was caused by a hybrid strain belonging to STEC O104:H4 that had aggR and *stx2a*.
eae	The *E. coli* attachment and effacing (*eae)* gene produces the virulence factor intimin that facilitates the attachment of *E. coli* to the human gut mucosa. STEC that have both *stx1a/2a/2c*/*2d*, and eae (or *stx1a* and eae in the case of STEC 026) are associated with the potential to cause severe disease or HUS.
Evidence of transmission	Evidence of person-to-person transmission may include symptomatic household or close contacts (including contacts in childcare settings for those aged 5 years old and under) during the case's infectious period, where STEC is the most likely cause of illness. Positive screening stool sample result for a household or close contact (including contacts in childcare settings for those aged 5 years old and under).
Haemolytic Uraemic Syndrome (HUS)	The clinical manifestation of acute kidney injury, thrombocytopenia and microangiopathic haemolytic anaemia, most commonly as a consequence of STEC infection. Up to 10% of STEC cases are estimated to develop HUS, although this may differ for cases of non-O157 STEC infection. Atypical HUS (also referred to as primary HUS) occurs without co-existing infection and is beyond the scope of this guidance.
Higher risk STEC strains (including	Higher risk STEC strains comprise:

Term	Definition
HUSEC, haemolytic uraemic syndrome Associated *E. Coli*)	• HUSEC (HUS-associated *E. coli*) strains, which usually express *stx2a* or *stx2d* Shiga together with *eae* or *aggR* virulence factors. These strains have a stronger association with HUS • other higher risk STEC, including STEC O26 and STEC expressing *stx2c* with *eae* or *aggR*. These strains are also associated with severe disease
Incubation period	The time period from exposure to STEC to onset of symptoms varies, depending upon the number of organisms ingested and host susceptibility. It has a reported range from 6 hours to 10 days, though 2 to 4 days is most common. For contact and source identification, the enhanced surveillance questionnaire (ESQ) routinely covers the period from 7 days before symptom onset; in some instances, the history may be extended up to 14 days at the discretion of the investigating team.
Infectious period	The period of highest infectiousness is presumed to last from onset of gastrointestinal symptoms until a minimum of 48 hours symptom free. Prolonged excretion of the organism can occur after symptom resolution, so microbiological clearance is recommended for groups that are at increased risk of spreading STEC infection.
Serogroup	Serogroup is the O (lipopolysaccharide) antigen, for example, O157
Serotype	Serotype is the combination of O (lipopolysaccharide) and H (flagella) antigen, for example, O157:H7
Shiga toxin (stx)	Stx1 was previously described as VT1 (verotoxin) Stx2 was previously described as VT2 (verotoxin)
Virulence profile	The combination of *stx* and *eae* genes detected by GBRU in-house PCR tests is currently the best indicator of the potential virulence of STEC, and its potential to cause serious illness including HUS.

The virulence profiles of STEC strains defined as higher and lower risk are summarised below. It should be noted that 'lower risk' does not imply no risk of potential to cause serious illness. Based on current evidence, public health action should be targeted towards higher risk STEC strains.

Virulence profiles of higher and lower risk non-O157 STEC strains					
Stage of algorithm	**Virulence profile**				**Description**
Stage 2 GBRU results In-house PCR	***stx1***	***stx2***	***eae***	**O26 PCR**	**Description**
	(+/-)	*(+/-)*	*(+)*	(+)	Higher risk: STEC O26
	(+/-)	(+)	(+)	(-)	Potential HUSEC
	(+)	(-)	(+)	(-)	Lower risk
	(+/-)	(+)	(-)	(-)	Lower risk

Stage 3 GBRU results WGS	***stx1* subtypes (any)**	***stx2* subtypes**	***eae***	***aggR***	**Description**
	(+/-)	*stx2a* or *stx2d*	(+/-)	(+/-)	Higher risk: HUSEC
	(+/-)	*stx2c*	(+/-)	(+/-)	Higher risk: other higher risk
	stx1a from O26	(+/-)	(+)	(+/-)	Higher risk: STEC O26
	(+)	(-)	(-)	(+/-)	Lower risk
	(+/-)	*stx2b* or *stx2e* or *stx2f or stx2g*	(+/-)	(+/-)	Lower risk

Introduction

The purpose of this guidance is to provide advice to public health practitioners on the public health management of Shiga toxin-producing *Escherichia coli* (*E. coli*) infections (STEC), also referred to as Verocytotoxin-producing *E. coli* (VTEC).

Diagnostic laboratories are required to notify UK Health Security Agency (UKHSA) health protection teams (HPTs) once identification of STEC has been made, according to the Health Protection (Notification) Regulations (2010). Similarly, cases where there is a clinical suspicion of haemolytic uraemic syndrome (HUS), regardless of whether there is microbiological evidence of an infectious cause, should be urgently notified to HPTs.

Historically, in the UK, diagnostic algorithms have focused on the detection of STEC O157:H7. This serotype is, therefore, the most frequently isolated. STEC other than serogroup O157 (non-O157 STEC) are under-ascertained but are now increasingly recognised for their ability to cause serious illness in infected individuals as well as their potential to cause outbreaks of infection.

This guidance is based on the available evidence for transmission and control of STEC infections and supersedes the 2011 Health Protection Agency VTEC Operational and Support manuals and 2018 PHE interim guidance. Clinical management of STEC cases is outside the remit of these guidelines.

Further public health guidance on the management of *E. coli* infections other than STEC can be found online.

Further guidance on gastrointestinal outbreak investigations, including references to relevant public health legislation, can be found online.

Main recommendations and changes

Recommendation	Change
Emphasis on higher risk STEC strains including HUSEC and STEC O26	Advice on new STEC O26 PCR assay from GBRU added. Definition of higher risk STEC clarified to include those associated with HUS and other forms of severe disease. Advice that lower risk STEC may still need to be managed as a high risk in some circumstances such as an outbreak.
Changes to contact definitions	Delineates household contacts, who are most likely to be at risk, from contacts in other circumstances, of greatest relevance in outbreaks.
Removal of serological testing advice	No longer performed by GBRU.
Simplified screening for asymptomatic contacts of higher risk STEC cases	Advises screening (but not necessarily exclusion) of household contacts where a case is identified at a late stage.
Clarified screening for HUS contacts without identified organism	Advises screening household contacts of cases with HUS without an identified organism to increase the likelihood of identification, and so guide public health management and diagnosis.
Combined guidance for STEC O157 and non-O157	Previously separate guidance combined for ease of reference.
Cases with prolonged excretion	Advice on risk assessment added.

Clinical enquiries relating to the specific management of cases and/or contacts should be directed to local HPT Gastrointestinal (GI) Leads or UKHSA national services, as usual.

Definitions for the public health management of STEC infections

Table 1. Definitions of cases of STEC infection

STEC case definition		Clinical features	Epidemiological link to a confirmed case	Laboratory findings	Action required
Confirmed (including STEC-related HUS)		Present or absent	Present or absent	GBRU Reference laboratory - positive STEC culture or PCR Shiga toxin positive	Initiate or continue public health action (see STEC algorithm)
		STEC-HUS	Present or absent	GBRU Reference laboratory - positive STEC culture or PCR Shiga toxin positive or Diagnostic laboratory – clinical diagnosis **and** PCR Shiga toxin positive	
PROBABLE	Local O157 culture positive	Present or absent	Present or absent	Diagnostic laboratory – positive culture presumptive STEC O157 regardless of PCR result	Initiate or continue public health action (see STEC algorithm) Initiate or complete reference laboratory testing
	Probable STEC-related HUS	HUS	Present or absent	Awaiting laboratory testing	
	Epidemiological link	Acute diarrhoea (may be bloody) present or absent	Present	Diagnostic laboratory – PCR Shiga toxin positive	
		Acute diarrhoea (may be bloody) present	Present	Awaiting laboratory testing	
	PCR probable	Bloody diarrhoea or hospitalisation for acute diarrhoea	Absent	Diagnostic laboratory – PCR Shiga toxin positive BUT negative culture for STEC O157	
POSSIBLE	Clinical possible	Bloody diarrhoea or hospitalisation for acute diarrhoea	Absent	Awaiting laboratory testing	Initiate or complete reference laboratory testing Send PCR letter and STEC leaflet (as guided by STEC algorithm)
	PCR possible	Absent (or symptomatic without bloody diarrhoea or hospitalisation)	Absent	Diagnostic laboratory – PCR Shiga toxin positive BUT negative culture for STEC O157	

Table 2. Contacts of a case of STEC infection

A contact is any person who is believed to have had significant risk of direct or indirect exposure to the excreta of an infectious person.

The ESQ asks for contact and exposure information in the incubation period (usually 7 days before symptom onset) in order check for common exposure cases, sources, and potential outbreaks.

Household

Someone who lives, or has stayed overnight, in the same household and ordinarily shares a bathroom or toilet facilities and ordinarily shares food with the case or had other significant close contact with the case (for example, sexual contact) during the infectious period.

In an outbreak scenario or where there is potential evidence of transmission outside the household, wider contact tracing may be considered in the following:

Food handling

Someone who has regularly eaten food prepared by the case or has eaten food prepared by the case on a single occasion during the infectious period if there is concern about hygiene practices of the case or if the case was symptomatic when preparing their food.

Caring duties

Someone who has been involved in nappy changing or toileting assistance of the case or who has been involved in close physical care of the case during the infectious period.

Shared exposure

Someone who has been exposed to the suspected or identified sources of infection. This may include children who have shared bathroom or toilet facilities with the case or have had close contact with the case in a childcare setting during the infectious period.

Table 3. Groups at risk for ongoing transmission of gastrointestinal (GI) infections

Risk group	Description	Additional comments
Group A	Any person who is unable to perform adequate personal hygiene due to their lack of capacity or ability to comply,or lack of access to hygiene facilities	Risk assessment should consider availability or access to toilets, handwashing or hand drying facilities in the work or educational setting
Group B	All children aged 5 years old or under (up to sixth birthday) who attend school, pre-school, nursery or other similar child care or minding groups	For children aged 5 years and under who do not attend school, risk assessment for clearance purposes should explore potential for transmission within other settings, for example, household or attendance at parties
Group C	People whose work involves preparing or serving unwrapped ready to eat food (including drink)	Consider informal food handlers, for example, someone who helps to prepare food for charity and community events
Group D	Clinical, social care or nursery staff who work with young children, the elderly, or any other particularly vulnerable people, and whose activities increase the risk of transferring infection via the faecal-oral route	Risk assessments should consider activities such as helping with feeding or handling objects that could be transferred to the mouth

Algorithms for the local response to cases of STEC infection

Since 2013, many local NHS laboratories have introduced real-time Polymerase Chain Reaction (PCR) testing as a gastrointestinal (GI) screening panel for faecal samples where infectious disease is suspected. These GI PCR panels include primers that detect Shiga toxin (*stx)* genes (*stx1* and *stx2)* that are possessed by all STEC. The introduction of *stx* PCR tests by a diagnostic laboratory is likely to lead to an increase in the number of STEC infections detected (O157 and non-O157) and consequently an increased number of notifications to local health protection teams (HPTs). Evidence of the public health impact of different non-O157 STEC is still emerging and a universal approach to the public health management of all *stx* positive results is not appropriate.

Local *stx* PCR positive but culture negative samples should be sent to the Gastrointestinal Bacteria Reference Unit (GBRU) for further investigation and for various non-O157 STEC serogroups to be identified. Referral of local culture negative samples is especially important for children, and those with bloody diarrhoea and haemolytic uraemic syndrome (HUS).

The ultimate aim of the public health response is to prevent disease and transmission associated with STEC infections. This is relatively rapid and straightforward for STEC O157 infections, because following an *stx* PCR positive result, local laboratories can proceed to test for and isolate O157 strains with reports of presumptive *E. coli* O157 infections usually available within 3 days of specimen collection, enabling the public health response to be commenced quickly.

Because *E. coli* O157 is not grown from the majority of *stx* PCR positive faecal specimens, and local laboratories cannot routinely isolate non-O157 STEC, there is a delay in full microbiological characterisation. Serotype and *stx* subtypes are usually reported by GBRU about 2 to 3 weeks after the HPT is first informed of the case.

Serotype is more readily available for STEC O26 (for which PCR testing has been implemented to provide a result 1 to 2 working days after the initial *stx* PCR profile). Like STEC O157, STEC O26 is more frequently associated with severe clinical outcomes, hospitalisation, and outbreaks in comparison to other STEC serotypes, and its isolation should prompt full public health actions.

The main aim of the public health response to non-O157 STEC is to prioritise the response to those cases most likely to be infected with viable STEC belonging to higher risk STEC strains, including STEC O26 and HUSEC strains. By doing so, this guidance seeks to provide a proportionate response that protects the public's health while taking into consideration the workload implications for HPTs or local authorities, without imposing unnecessary restrictions on individuals.

While full characterisation of an STEC isolate is pending, local PCR and culture results, followed by GBRU in-house PCR results may be available. The following algorithms have therefore been divided into 3 stages based on this process to provide HPTs with guidance on how to respond to cases as each new piece of information becomes available.

The 3 algorithms are based on laboratory results as they become available, as follows:

- Stage 1 - Diagnostic laboratory results (PCR and culture), age of the case, and clinical history (HUS or bloody diarrhoea)
- Stage 2 – GBRU in-house PCR results (stx and E. coli attachment and effacing (eae) gene, plus STEC O26 identification)
- Stage 3 – GBRU serogroup or serotype including stx subtypes

The algorithms should be used for the investigation of single cases and is colour coded for public health management as follows:

- red border – full or majority of public health actions recommended
- amber border – limited public health actions recommended
- green border – warn and inform public health actions only, or no public health actions
- blue background – questions for decision-making process
- white – information only

Notes provide guidance and follow each stage in the algorithm.

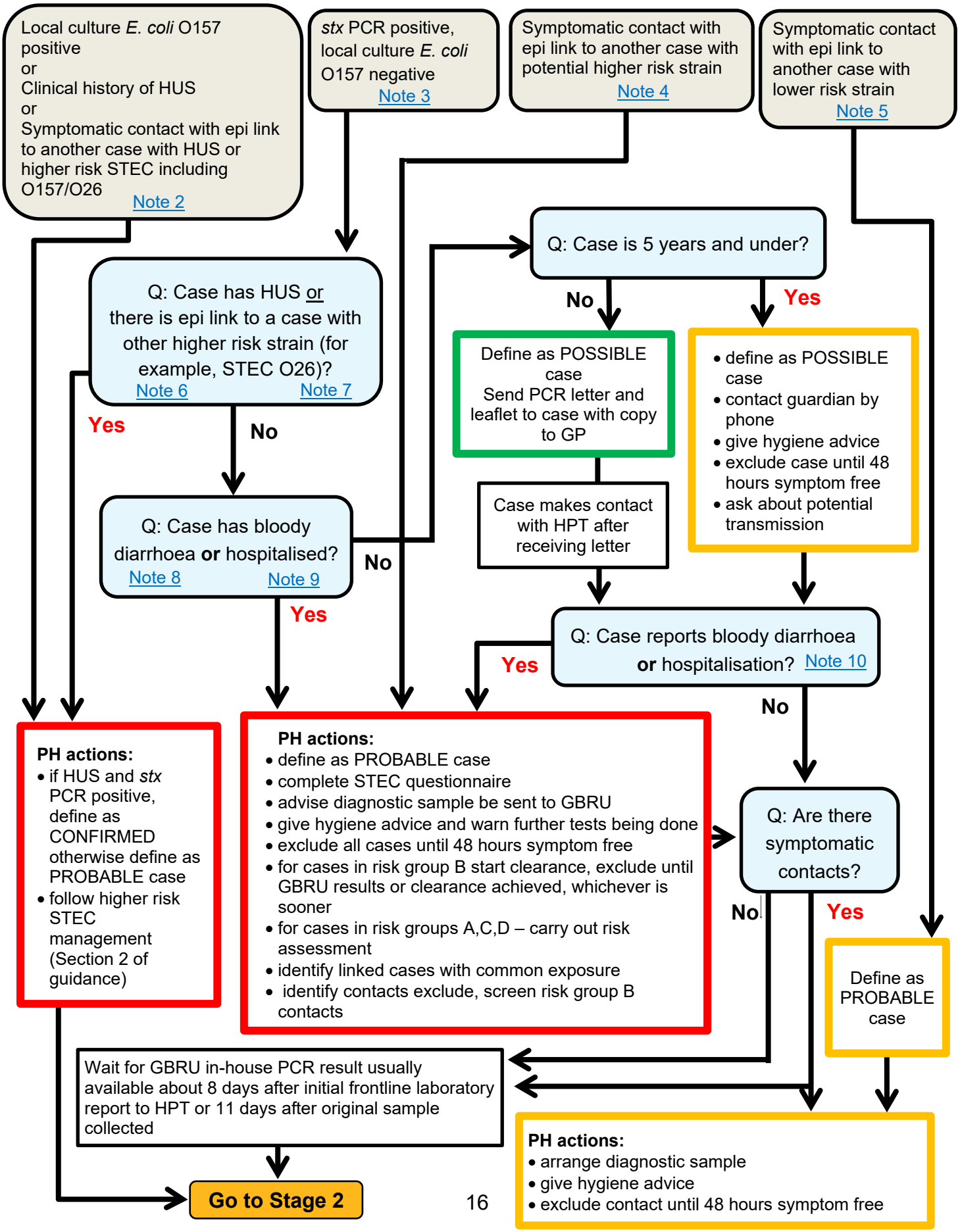
The algorithms should be used in conjunction with the following sections of this guidance as appropriate:

- Section 2. Public health management of STEC O157 and non-O157
- Section 3. Outbreaks and clusters

Accessible text-only versions of the algorithms are available in Appendix C.

Stage 1 STEC ALGORITHM

Note 1



Stage 1. Diagnostic laboratory results and clinical history

Note 1

There are several ways potential STEC infections are reported to the HPT:

- local culture *E. coli* O157 positive
- notification of HUS
- symptomatic contact with an epidemiological link to another case with HUS, or culture confirmed O157 STEC, or culture confirmed non-O157 STEC belonging to a higher risk strain (*stx2a/2c/2d* and *eae/aggR* positive or STEC O26)
- local *stx* PCR positive, but local culture negative for *E. coli* O157
- symptomatic contact with an epidemiological link to another case with culture-confirmed potential higher risk strain (*stx2* and *eae*)
- symptomatic contact with an epidemiological link to another case infected with culture confirmed lower risk STEC strain (non *stx2a/2c/2d*)

For notifications of infective bloody diarrhoea, unless there is a known epidemiological link to a case with potential or confirmed higher risk STEC infection, public health action can usually wait until the local diagnostic laboratory culture results are known. If local laboratories are using PCR, initiation of public health action should follow locally agreed arrangements.

Note 2

Local culture *E. coli* O157 positive or history of HUS

- define case as probable
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale
Most cases of diarrhoea associated HUS are caused by STEC belonging to HUSEC strains.

Symptomatic contact with an epidemiological link to another case with HUS, or culture confirmed STEC of a higher risk strain, including O157, O26, and/or strains with a higher risk virulence profile (*stx2a/2c/2d* and *eae/aggR*)

- define case as probable
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale
There is evidence of potential transmission of higher risk strain between the case and this symptomatic contact.

Note 3

Local *stx* PCR positive, local culture *E. coli* O157 negative

This is the usual result received by HPT and is the usual starting point of the response. Result may be received by phone call or SGSS import to HPZONE:

- clinical and demographic information should be reviewed
- if positive PCR results are received while local culture results are pending, it may be appropriate to commence public health actions, then to follow the relevant arm of the algorithm once culture results are available

Rationale
Stx PCR tests are highly sensitive and specific, but do not distinguish between viable and non-viable organisms or even free *stx*-bacteriophages in the faeces.

Note 4

Symptomatic contact with an epidemiological link to another case with a potential higher risk strain (*stx2* and *eae* regardless of *stx1*)

- follow the actions for cases with history of bloody diarrhoea (Note 8)

Rationale
The case associated with this symptomatic contact may not subsequently be confirmed by GBRU to be a higher risk strain. Advice to implement pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and complete the STEC questionnaire (information about potential transmission and contacts) aims to balance the risk of transmission against imposing restrictions on the case that may not be necessary.

Note 5

Symptomatic contact with an epidemiological link to another case with lower risk strain (non *stx2a/2c/2d)*

Define case as probable and:

- arrange diagnostic sample, give hygiene advice, provide PCR letter or leaflet if not already done and exclude until minimum of 48 hours symptom free
- public health actions determined by diagnostic result

Rationale
There is an epi link is to another case with a lower risk strain. The likelihood of serious illness or outbreaks is low. Manage like other non STEC gastrointestinal infections.

Note 6

Local *stx* PCR positive, local culture *E. coli* O157 negative with history of HUS or epidemiological link to case infected with a higher risk strain (HUSEC/STEC O26)

- *Stx* PCR positive and HUS: define case as confirmed, or
- epidemiological link: define case as probable
- full public health actions as per higher risk STEC management for case and contacts are recommended

Rationale

- current case is *stx* PCR positive and is a contact of another case infected with a higher risk strain
- there is evidence of possible transmission
- or a case of diarrhoea-associated HUS, most of which are caused by a higher risk strain of STEC

Note 7

Local *stx* PCR positive, local culture *E. coli* O157 negative no history of HUS and no epidemiological link to case infected with a higher risk strain

- review history for features of severe disease – bloody diarrhoea or admission for acute diarrhoeal illness. Depending on local arrangements, this information may be on laboratory request form or provided by reporting clinician or microbiologist
- in the absence of this information, the HPT should consider contacting the clinician who arranged for the test to confirm the history

Note 8

Local *stx* PCR positive, local culture *E. coli* O157 negative with history of bloody diarrhoea

History of bloody diarrhoea or admission with acute diarrhoeal illness has been reported on the laboratory result report or by the clinician or microbiologist:

- define case as probable
- complete STEC questionnaire
- provide hygiene advice (written if possible) and warn case that further tests are being done on the sample
- exclude all cases until 48 hours symptom free

- if case is in risk group B consider commencing clearance once 48 hours symptom free and exclude until GBRU in-house PCR is known or clearance achieved, whichever is sooner (see Table 6)
- if case is in risk group A, C, D do not automatically exclude case: carry out risk assessment (see Table 6)
- identify any linked cases resulting from a common exposure
- if there are symptomatic contacts arrange single diagnostic sample, give hygiene advice and exclude them until 48 hours symptom free
- exclude and screen risk group B contacts
- wait for GBRU in-house PCR result, available around 11 days after sample collected before starting public health actions for asymptomatic contacts in risk groups A to D (see Table 7)

Rationale
Although the case has bloody diarrhoea, most isolates are not subsequently confirmed by GBRU to be viable STEC belonging to higher risk strains. However, bloody diarrhoea is more frequently associated with infection with higher risk strains. Advice to implement pragmatic precautions (exclusion while symptomatic and providing hygiene advice) and complete the STEC questionnaire (information about potential transmission and contacts) aims to balance the risk of transmission against imposing restrictions on the case that may not be necessary.

Note 9

Local *stx* PCR positive, local culture *E. coli* O157 negative no evidence of severe illness

Where there is no evidence of severe illness:

- define case as possible
- if the case is aged 5 years and under it is recommended to make contact by phone with parent or guardian to confirm history and carry out a rapid risk assessment (see Appendix A2)
- provide written information to case (or parent or guardian) and copy to the GP (see Appendices A3 and 4)
- no other public health actions recommended at this stage
- wait for GBRU in-house PCR and culture results

Rationale
Young children are particularly susceptible to acquiring and transmitting STEC infections and that they are also at greater risk of developing severe infection such as HUS.

Note 10

Local *stx* PCR positive, local culture *E. coli* O157 negative patient reports bloody diarrhoea

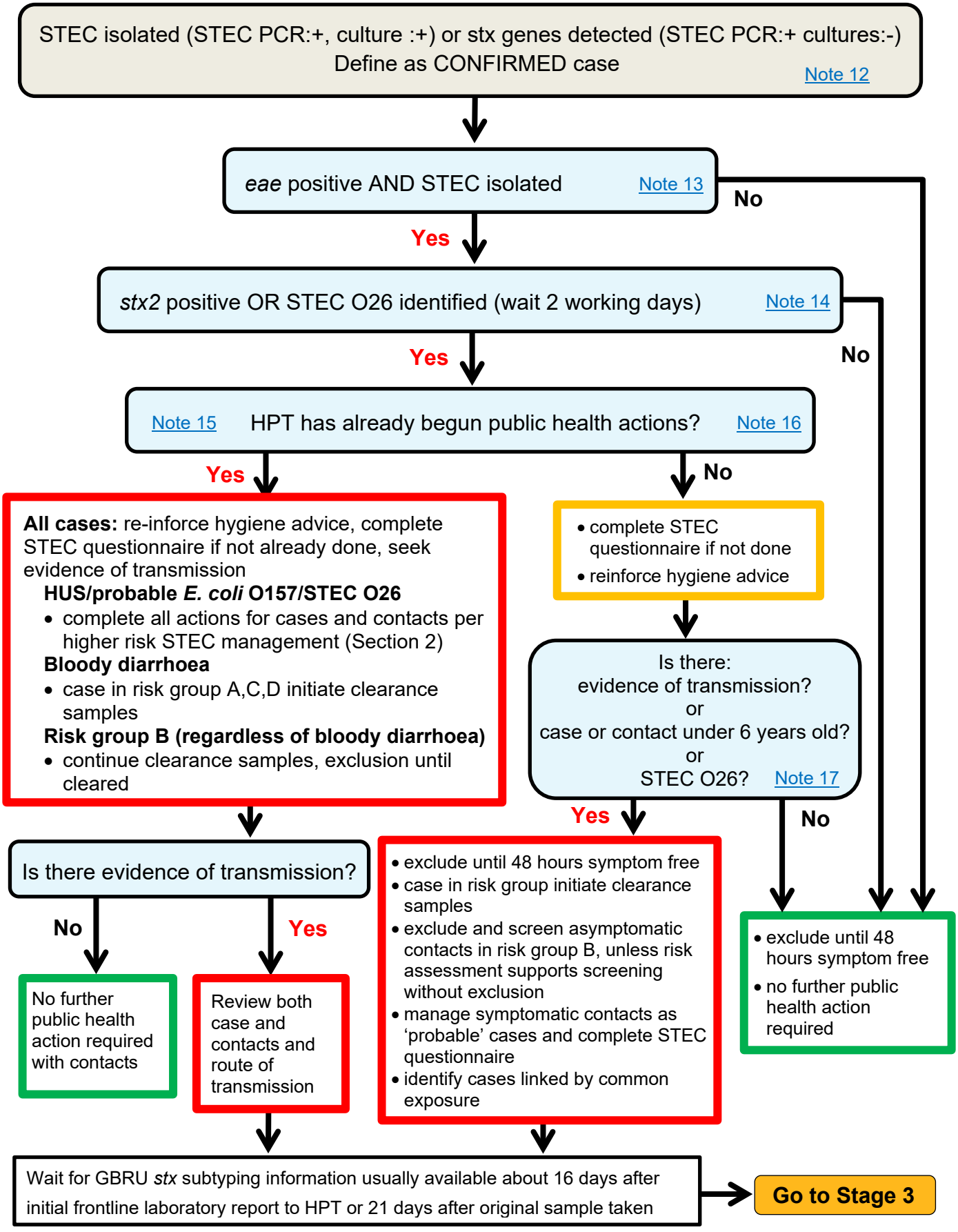
If case makes contact with HPT and reports bloody diarrhoea or admission with acute diarrhoeal illness:

- manage as a potential higher risk strain as per Note 8, above

If case reports that contacts have been symptomatic:

- arrange single diagnostic sample per contact, give hygiene advice and exclude contact until 48 hours symptom free

Stage 2 GBRU in-house PCR result Note 11



Stage 2. GBRU in-house PCR results (stx, eae, and O26)

Note 11

Detection of *stx* and *eae* genes in a specimen does not indicate the viability of the organism. It is the combination of both *stx* and *eae* gene profile and culture result from GBRU which is most useful in directing public health actions. In stage 2, the possession of *stx2* and *eae* is used to identify infections caused by potential higher risk strains. Additional measures are recommended where STEC O26 is identified, as it is associated with severe disease (with *stx1* or *stx2*) and can be identified by GBRU at this stage.

Note 12

GBRU in-house PCR results

At this stage the GBRU in-house PCR results are reported on GDW2 and include the *stx* and *eae* results (see Appendix 1):

- STEC isolated (STEC PCR:+ culture:+) – this indicates that STEC is present and viable, and an isolate is available for WGS
- stx genes detected (STEC PCR:+ culture:-) – this indicates that STEC is present, but the organism is not viable, or the numbers are too low to isolate
- STEC NOT isolated (STEC PCR:- culture:-) – this indicates that STEC is not present

Notes on PCR results

About 30 to 40% of *stx* PCR positive results are not confirmed by GBRU; this is because:

- DNA degrades quickly in faecal samples, the inherent turn-around time between local lab testing and GBRU testing can affect detection
- local diagnostic laboratories perform direct DNA extraction from the sample, whereas GBRU does an overnight broth enrichment step. If the bacteria are viable and multiply, the enrichment step increases the amount of DNA present; if the bacteria are dead, enrichment dilutes the DNA
- pathogens are not evenly distributed throughout a faecal sample

Be aware that the PCR result is from DNA extracted from a faecal sample. The combination of positive *stx1/stx2/eae* genes may be derived from more than one strain of STEC and non-STEC pathogens in that sample.

Note 13

eae positive and STEC isolated (culture positive)

- for all combinations of stx1 and/or stx2 with positive eae results, change case definition to confirmed
- for all eae negative cases, there are no public health actions (until Stage 3 results are known) beyond ensuring the case is excluded until 48 hours symptom free
- if STEC is not isolated, there are no public health actions routinely recommended (until Stage 3 results are known) beyond ensuring case is excluded until 48 hours symptom free

Note 14

Stx2 positive or STEC O26 identified

At the reference lab, a new PCR test has been added as an additional step to identify serogroup O26:H11 after STEC is isolated by culture. HPTs are advised to wait 2 working days after culture and *stx* results, especially for *stx1* and *eae*-positive cases. If O26 is not positive at that point, public health actions already commenced can be stopped.

- culture-positive STEC with stx2 and eae is a potential higher risk strain
- all STEC O26 cases should be followed up, regardless of stx/eae gene profile
- in summary, if the result is positive for both stx2 and eae, and organism is viable or STEC O26 is identified (regardless of stx/eae profile), go to the next question in the algorithm
- if stx2 is negative and STEC O26 is not identified after 2 working days, there are no public health actions routinely recommended until Stage 3 beyond ensuring the case is excluded until 48 hours symptom free

Note 15

Case is already known to HPT and public health actions have been commenced

For cases with a history of HUS or probable E. coli O157, full public health actions are likely to have begun, and may have been completed, prior to the GBRU PCR result. If there is a history of bloody diarrhoea, some public health actions are likely to have begun, particularly if the case is in a risk group.

All cases:

- change case definition to confirmed
- re-assess evidence of transmission (given that, potentially, a further incubation period has passed since initial contact with the case) and screen and exclude contacts in risk group B if not already commenced

HUS or probable *E. coli* O157/O26:

- all actions as per higher risk STEC management should have been completed or are in progress, including providing advice and the possible exclusion and screening of contacts (see Table 7)

Cases with bloody diarrhoea. Review public health actions, including providing advice and the possible exclusion and screening of:

- asymptomatic contacts in risk groups A, C, D (Note 8) (Table 7)
- symptomatic contacts (see Table 7)

Children under 6 years of age (risk group B) regardless of symptoms:

- if already excluded, continue until clearance has been achieved
- if not already excluded, carry out risk assessment to determine need for exclusion until clearance has been achieved (see Table 6). However, if there is evidence of transmission exclude until cleared

Rationale
The STEC is viable and a potential higher risk strain. It may not have produced serious symptoms in this case, but if the case is shedding, there is still the potential for transmission, particularly if the case is a young child. Some strains appear to cause more severe disease in secondary cases.

Note 16

Public health actions not started

If the HPT was not previously aware of the case, but identified it from GDW2 or if, from initial clinical history, the case had been assessed to be lower risk:

- case is defined as confirmed
- complete the STEC questionnaire if not already done
- re-enforce hygiene advice that may have been provided to the case in the letter or leaflet
- assess for evidence of transmission:
    - if there is no evidence of transmission, exclude case until 48 hours symptom free, but there are no further public health actions for the case or their contacts
    - if there is evidence of transmission, then follow up is recommended

Rationale
This case is infected with a potential higher risk strain (serotype and *stx2* subtype not yet known). An assessment of potential transmissibility is advised, even though the strain has not caused severe illness in this case.

Note 17

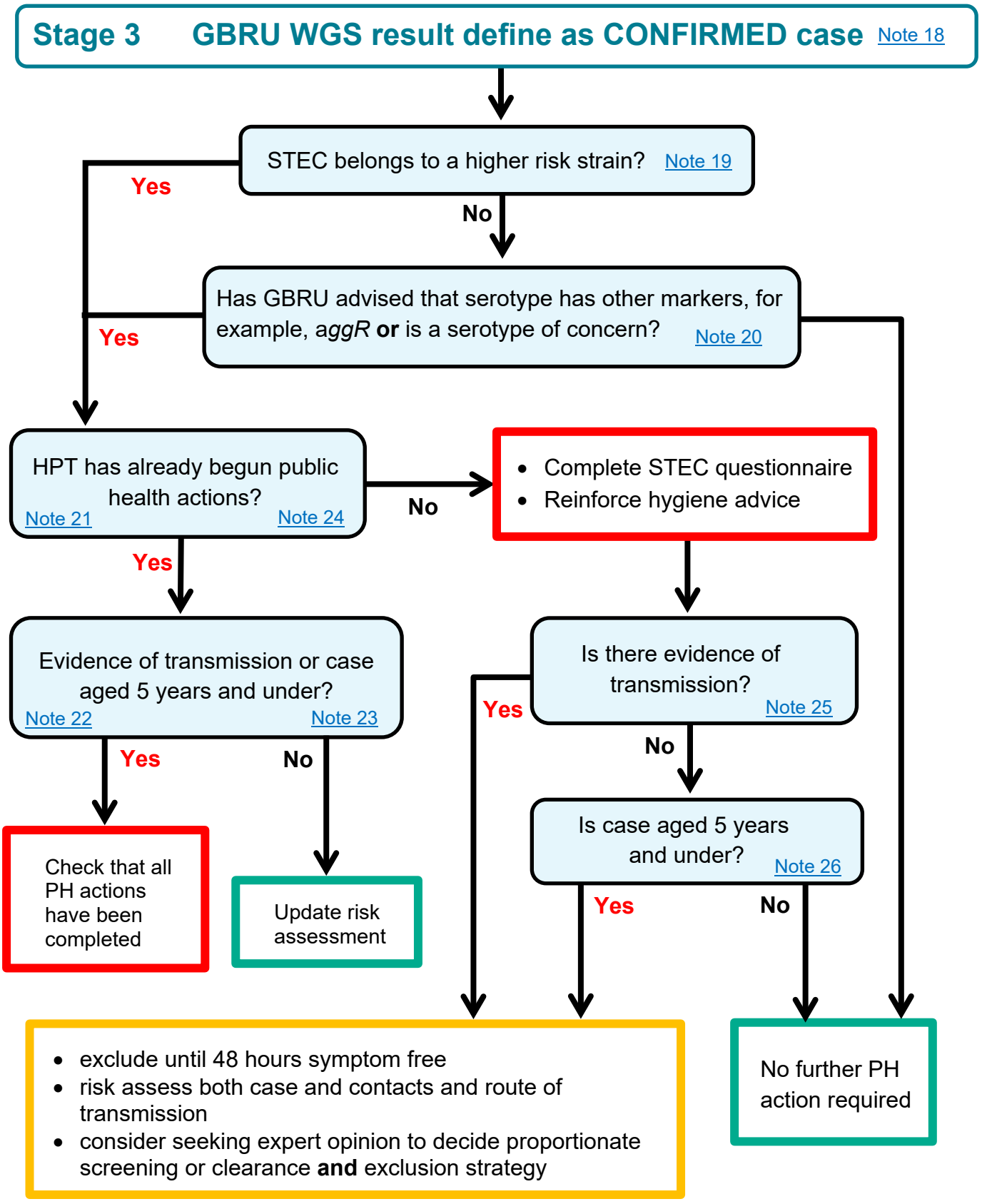
Assess if:

- evidence of transmission
- age 5 or under (case or household contact)
- STEC 026 identified

If any of the above apply:

- if case is in risk group B, carry out risk assessment to determine need for exclusion until clearance has been achieved (Table 6). However, if there is evidence of transmission, exclude until cleared
- if case is in risk group A, C, D, carry out risk assessment to determine need for exclusion until clearance has been achieved (Table 6)
- asymptomatic contacts in risk group B: exclusion and clearance recommended. Risk assessment to determine need for exclusion may be considered (Table 7). If there is difficulty in obtaining a screening sample or evidence of transmission, exclude until screened
- asymptomatic contacts in risk group A, C, D: screening not recommended (Table 7)
- symptomatic contacts:
    - manage as a probable case
    - arrange single diagnostic specimen and exclude until 48 hours symptom free
    - if symptomatic contact is in risk group A to D continue to exclude until the diagnostic or screening result is known (Table 7)

Rationale
Children aged 5 years and under can shed STEC for prolonged periods, and onwards transmission is not uncommon. If a case has symptomatic contacts, assume that transmission may have occurred.


Stage 3 GBRU WGS result define as CONFIRMED case Note 18
STEC belongs to a higher risk strain? Note 19
Yes
No
Has GBRU advised that serotype has other markers, for example, aggR or is a serotype of concern? Note 20
Yes
HPT has already begun public health actions? Note 21 Note 24
No
Complete STEC questionnaire
Reinforce hygiene advice
Yes
Evidence of transmission or case aged 5 years and under? Note 22 Note 23
Yes
No
Check that all PH actions have been completed
Update risk assessment
Is there evidence of transmission? Note 25
Yes
No
Is case aged 5 years and under? Note 26
Yes
No
exclude until 48 hours symptom free
risk assess both case and contacts and route of transmission
consider seeking expert opinion to decide proportionate screening or clearance and exclusion strategy
No further PH action required

Stage 3. GBRU serogroup or serotype including stx subtypes

Note 18

GBRU WGS results

- define case as confirmed (if case not previously reported)

Rationale
The *stx* subtypes *stx2a/stx2c/stx2d* are strongly associated with risk of severe disease including HUS, particularly if positive for *eae* or *aggR* gene (as reported in GDW2).

Note 19

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain)

- it is recommended that all isolates with *stx2a/2c/2d* regardless of *eae* should be followed up for public health action
- GBRU provides the *aggR* result on GDW2
- all STEC O26 cases should be followed up, even with a non HUSEC profile

Note 20

Serotype has a lower risk strain profile

It is probable that, in future, other pathogenic strains will emerge and GBRU will alert HPTs if additional actions are recommended.

Rationale
Bacteria are constantly evolving there have been documented instances when an *E. coli* strain of low pathogenicity has acquired *stx* genes, or where new evidence has implicated a serotype or genotype in severe disease (for example, increased severe disease associated with STEC O26:H11, and a Europe-wide outbreak of HUS and other severe disease associated with EAEC O104:H4.

Note 21

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the HPT has commenced public health actions

If the strain has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the STEC questionnaire has already been completed:

- for cases with HUS, bloody diarrhoea or probable STEC O157/ STEC O26, public health actions will probably have been completed

- check that all public health actions have been completed
- for cases in risk groups, it is possible that there may be some outstanding public health actions, particularly if the initial GBRU result in Stage 2 was stx2 but negative for eae:
    - review public health actions already completed, and complete STEC questionnaire if not already done
    - review risk assessment: consider the time period since original sample was submitted or disease onset date
- for all other cases, there are no further public health actions

Note 22

Case in risk group B **or** there is evidence of transmission

If there is evidence of transmission or the case is in risk group B:

- review all public health actions to ensure that they have been completed
- if no evidence of transmission, close case

Note 23

Case not in risk group B and no evidence of transmission

- if there is no evidence of transmission and the case is not in risk group there are no further public health actions
- if the case is in risk group A, C or D, follow guidance in Table 6

Note 24

Serotype has the *stx* subtype *stx2a/2c/2d* (higher risk strain) and the HPT has not begun public health response

For all cases:

- complete the STEC questionnaire
- reinforce hygiene advice verbally and in writing

If there is evidence of transmission:

- exclude case and symptomatic contacts until 48 hours symptom free
- complete risk assessment for case and symptomatic contacts and potential route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted or disease onset date, and risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

Note 25

There is evidence of transmission

- exclude case and symptomatic contacts until 48 hours symptom free
- complete risk assessment for case and symptomatic contacts and potential route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted or disease onset date, and risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

Note 26

Risk group B and no evidence of transmission

- exclude case until 48 hours symptom free
- complete risk assessment for case and contacts and route of transmission
- consider obtaining expert opinion from GBRU, taking into account the risk presented by the serotype, the time period since original sample was submitted or disease onset date, and risk assessment information for both case and symptomatic contacts to determine if further public health actions are recommended

1. General information on the public health management of STEC infections

1.1 Microbiological diagnosis and confirmation

Diagnostic laboratories should investigate all diarrhoeal specimens for the presence of STEC, using the procedures recommended in the UK Standards for Microbiology Investigations - Investigation of faecal specimens for enteric pathogens (1). Diagnostic laboratories routinely test for *E. coli* O157.

Specific procedures used by local diagnostic laboratories may vary. However, most will perform faecal culture, a biochemical identification of *E. coli*, and a slide agglutination (or latex kit) test to identify *E. coli* O157.

Diagnostic laboratories should refer samples to the Gastrointestinal Bacteria Reference Unit (GBRU) for further testing and confirmation as follows:

A) Cases of HUS

1. Laboratories using culture-based methods for detection of STEC should refer faecal specimens from cases of HUS on the day of receipt to GBRU. If no faecal specimens are available, a rectal swab may be performed to avoid delay.
2. Laboratories using PCR or enzyme-linked immunoabsorbent assay (EIA) for detection of STEC should refer all positive faecal specimens from cases of HUS urgently to GBRU to optimise isolation (non-O157 and O157 STEC), characterisation of virulence and typing.
3. Faecal samples should also be taken from household members, to improve the chances of diagnosis and aid public health management (see Section 2.1.1).
4. If all samples (including household samples) are negative, the case may have had STEC infection which was not detected microbiologically (particularly where antibiotics were given prior to specimen collection), or may have a non-infectious aetiology (atypical HUS). Even if there is a clinical diagnosis of atypical HUS, it may be appropriate to take public health actions, guided by the age of the case, previous antibiotic use, or other factors that might increase the likelihood of undetected STEC infection.

B) Cases without HUS

1. Presumptive (locally confirmed) isolates of *E. coli* O157 for confirmation of identity, Shiga toxin gene detection and serotyping by PCR, and whole genome sequencing to determine the single nucleotide polymorphism (SNP) profile.

2. Faecal samples testing positive for *stx* by PCR in local diagnostic laboratories where commercial PCR assays for gastrointestinal infections are used routinely and are culture negative locally for presumptive *E. coli* O157, particularly if the case is aged 5 years old or under or was admitted due to the severity of the diarrhoeal illness.
3. Other strains of *E. coli* for confirmation of identity and Shiga toxin gene detection if there is a high clinical suspicion of STEC infection.
4. Faecal specimens from cases with bloody diarrhoea in whom conventional laboratory testing has failed to yield presumptive *E. coli* O157 or any other pathogen.
5. Faecal samples from symptomatic contacts of cases of STEC infection or any STEC outbreak-associated case in whom conventional culture laboratory testing has failed to yield a pathogen. These should be discussed with GBRU prior to submission to ensure there is capacity for testing;

Confirmatory PCR results are available for isolates sent to GBRU on the date of receipt and phage typing results for STEC O157 are available within 2 working days of GBRU receipt, typically about 11 days from the date the sample was collected. Serotyping for non-O157 STEC information from GBRU is generally reported 8 to 12 days from the date of receipt, typically about 21 days after the sample was collected. STEC O26 can be identified by PCR of specimens sent to GBRU, and results are generally available within 2 working days of the initial *stx* and *eae* profile.

Clearance and screening samples (as outlined in Section 2 of this guidance) should be submitted to a UKHSA regional laboratory. Where contacts are symptomatic, ensure their GPs are informed, an assessment of the contacts' clinical condition is completed, and samples are submitted for diagnosis.

1.2 Notification of STEC infections

Diagnostic laboratories should notify UKHSA HPTs once a presumptive identification of STEC has been made, according to the Health Protection (Notification) Regulations (2010). This should be done at least verbally within 24 hours and followed up by written notification within 7 days. In order to enable urgent public health actions to be commenced, diagnostic laboratories should notify the local HPT of the following:

- presumptive (locally confirmed) isolates (see Appendix B. Microbiological diagnosis)
- detection of *stx* DNA from faeces via PCR methods (*stx* PCR positive)

Prompt notification of cases of STEC infection – and cases where there is a clinical suspicion of HUS regardless of whether or not there is microbiological confirmation of an infectious cause – is required to facilitate the commencement of public health action to prevent further cases and interrupt transmission. Clinical notification should be made the same day, including out of hours, by telephone to the appropriate HPT.

HPTs may be notified of cases of STEC infection via the following routes:

- formal notification by a registered medical practitioner (RMP), such as a GP or hospital clinician. Haemolytic uraemic syndrome (HUS) and infectious bloody diarrhoea are notifiable by RMPs under the Health Protection (Notification) Regulations 2010
- laboratory notification of the identified organism from a local diagnostic or national reference laboratory

At the time of notification, in addition to the legally required demographic data about the case, the following information, if available, will assist in guiding public health action:

- clinical picture – including symptoms (bloody diarrhoea, HUS) and their onset date. Hospitalisation may be an indication of illness severity
- known epidemiological link – this will be particularly important for RMP notifications of infectious bloody diarrhoea to distinguish between possible and probable cases
- laboratory investigations – results of completed investigations and ensure appropriate testing for STEC infections is underway (including local and reference laboratory testing as appropriate)

The public health management of cases of STEC infection will be guided by whether a case meets the definition of a possible, probable or confirmed case as detailed in Table 1.

1.3 General principles of public health management

The following section outlines the general principles of the public health management of STEC infections.

Enhanced surveillance questionnaire

The STEC enhanced surveillance questionnaire should be completed for all relevant cases to enable a detailed history to be obtained for the 7 days prior to onset of illness.[1]

Please use the current version of the questionnaire.

The surveillance questionnaire should be completed within 24 hours of the notification of a probable or confirmed case to the HPT. Completion of the questionnaire by HPTs or Environmental Health Officers (EHOs) will depend on local arrangements. If the case is notified

[1] The incubation period for STEC is usually 2 to 4 days so obtaining information on potential exposures in the 7 days prior to illness should capture most potential exposures. However, occasional reports of the incubation period being up to 14 days do exist so in some instances the history may be extended up to 14 days at the discretion of the investigating team.

out of hours, as a minimum, a rapid risk assessment by phone is recommended (see Appendix A2) and the full questionnaire should be completed the next working day.

Completed questionnaires should be submitted promptly to national gastrointestinal teams via secure email to: vtec@phe.gov.uk

Risk assessment

An appropriate risk assessment of cases and their contacts should be conducted depending on the case definition and laboratory results as detailed in Section 2 of this guidance. This may be conducted by HPTs or the local environmental health (EH) department depending on local arrangements.

An STEC risk assessment proforma may be found in Appendix A2 of this document. The information that may be required includes:

- clinical condition including symptoms, symptom onset and duration
- identify links to known cases, outbreaks or suspected outbreaks
- determine whether case and/or contacts belong to a group at higher risk for ongoing transmission of gastrointestinal infections (see Table 3)
- establish hygiene standards and facilities which may help support measures to reduce secondary transmission
- obtain details of contacts for assessment of need for public health action

Control measures

Provision of information and hygiene advice:
Cases should be provided with appropriate information and hygiene advice to prevent the onward transmission of STEC infections.

Information on STEC can be found on the UKHSA website and on the NHS Choices website.

Exclusion and clearance samples for cases:

For probable and confirmed cases, recommendations for exclusion and microbiological clearance should be commenced following completion of the initial risk assessment per algorithms 1 to 3 of this guidance.

The local authority has statutory powers within the Public Health (Control of Disease) Act 1984 (as amended) (2) and the accompanying Health Protection (Local Authority Powers) Regulations 2010 (3). Guidance on the use of these provisions has been issued jointly by the HPA, then PHE (now UK HSA) and Chartered Institute of Environmental Health (CIEH) and Lewes District Council (4). Exclusion may be arranged, either by the local authority where the case is resident, or by the local authority where they are in employment.

The schedule of exclusion and clearance for individual cases and/or screening of contacts should be agreed between HPTs and EH departments and should be shared with cases and their families to support any ongoing public health actions required.

Contact identification and management

Close contacts of cases may need to be identified and managed as detailed in algorithms 1 to 3 and sections 2 and 3.

Communication and governance

Relevant organisations and/or persons should be advised of probable and confirmed cases of STEC infection to support prevention and control measures. These may include the following:

General practitioners (GPs)

If not already aware of the diagnosis, GPs of probable and confirmed cases should be advised of the suspected or confirmed diagnosis of STEC infection as detailed in algorithms 1 to 3 and sections 2 and 3. They may be provided with information on STEC infection, including guidance for exclusion and microbiological testing.

The use of antibiotics and antidiarrheal medications is not generally recommended in the management of STEC infection due to an increased risk of HUS.

Specific guidance relating to the management of acute bloody diarrhoea in children is available and GPs should be reminded to seek specialist support for any child presenting with a single acute episode of bloody diarrhoea. Guidance is available on the UKHSA website.

Environmental health (EH) departments

Local EH teams should be advised of probable and confirmed STEC cases as detailed in algorithms 1 to 3 and sections 2 and 3.

Risk assessments, microbiological clearance and screening samples and investigations of potential sources of exposure should be conducted according to local agreements. Local authorities, rather than UKHSA, have the legal powers for exclusion.

Local authority public health teams

Reporting arrangements to local authority public health teams should be agreed locally. These may include notification of cases in schools or childcare settings or suspected or known clusters or outbreaks.

UKHSA services

Other local HPTs should be informed of any potential exposures or links to cases in other areas for local risk assessment and management.

National Infection Services teams should be advised of probable and confirmed cases as detailed in algorithms 1 to 3 and sections 2 and 3 for the purposes of surveillance and further investigation and management as needed.

Media

Communications departments should be notified according to local agreements. These may include UKHSA, local authority and local NHS communications teams. This may be especially relevant if there are features of the case that may attract attention, such as severe illness or death, association with other cases or potential exposures, or socially sensitive settings such as nurseries or schools.

2. Public health management of STEC (O157 and non-O157)

2.1 The aims of public health management of STEC

There is consensus that HPTs should target their public health actions to cases from whom STEC organisms have been isolated and belong to higher risk strains (including O157 and O26), which are associated with severe infections including HUS and bloody diarrhoea.

It is recommended that faecal specimens from a case that are PCR-positive culture-negative for STEC when tested at the local hospital diagnostic laboratory are referred to GBRU for PCR and culture. For faecal specimens that are negative for STEC or confirmed by PCR only at GBRU, it is reasonable to assume that the case is no longer infectious and unlikely to transmit the infection, because STEC is no longer viable or present in very low concentration. This pragmatic approach means that only about 30% of *stx* PCR positive reports will require public health action when all microbiological tests have been completed (5). However, it does presume that, in addition to notifying the local HPTs, the local diagnostic laboratories submit samples that are *stx* PCR positive to GBRU for confirmation – at least for cases with HUS, bloody diarrhoea, or those who are aged 5 years and under.

If local diagnostic laboratories do not routinely send *stx* PCR positive, local culture STEC O157 negative samples to GBRU, HPTs are advised to agree criteria with the laboratories for doing so.

Suggested criteria:

- cases with HUS
- cases with bloody diarrhoea (with no other obvious cause)
- cases hospitalized with acute diarrhoeal illness
- cases aged 5 years and under (up to their sixth birthday)
- HPT has information to suggest there is evidence of transmission or a potential outbreak

It is also important to ensure these PCR-positive cases are recorded on SGSS in the correct manner, to ensure they are captured by the surveillance system.

The ultimate aim of the public health response is to prevent disease and transmission associated with STEC infections. This is relatively rapid and straightforward for STEC O157 infections, because following an stx PCR positive result, local diagnostic laboratories can proceed to isolate and test for *E. coli* O157. For such cases, HPTs will usually receive reports of

presumptive *E. coli* O157 infections within 3 days of specimen collection. The public health response can be commenced quickly, and most isolates will be confirmed by GBRU to be STEC O157.

For the majority of stx PCR positive specimens, *E. coli* O157 is not isolated. Because local diagnostic laboratories cannot routinely isolate non-O157 STEC, identification takes longer, and requires reference laboratory confirmation. For such cases, the public health response aims to prioritise cases that are most likely to be infected with viable STEC belonging to a higher risk strain, or another strain of concern (in particular, STEC O26). The response also aims to minimise unnecessary public health actions, including microbiological clearance, screening of contacts and exclusion from education or work. Such interventions can impose a considerable burden, including financial, on cases and their households, and so are most appropriate where the risk is highest.

Bloody diarrhoea (due to haemorrhagic colitis), HUS, and possibly admission due to acute diarrhoeal illness are associated with STEC infection caused by higher risk strains (including O157 and O26). Children aged 5 years and under are more vulnerable to severe illness, and more likely to acquire and transmit infection.

HPTs should review the available clinical information for cases that are stx PCR positive. This may be obtained from a variety of sources (depending upon local arrangements), such as telephone notification, laboratory request forms, or information from the referring clinician, or parents of children aged 5 years and under.

2.2 Public health management of POSSIBLE STEC cases (O157 and non-O157)

Cases may be defined as possible STEC on the basis of their clinical, epidemiological and laboratory findings, as defined in Table 1. The public health actions for such cases are summarised in Table 4.

Table 4. Public health management of possible STEC cases

Case definition	Public health action
Clinical possible case	• diagnostic laboratories should initiate or complete diagnostic testing, notify HPT if presumptive O157 and ensure samples or isolates are sent to the GBRU as appropriate • clinician to advise exclusion until 48 hours symptom free • no further public health action is required until results of microbiological testing are available
PCR possible case	• diagnostic laboratories should initiate/complete diagnostic testing, notify HPT if *stx* PCR positive and culture negative for O157, and ensure samples or isolates are sent to the GBRU as appropriate • clinician to advise exclusion until 48 hours symptom free • HPTs to review clinical history. Send written information to all cases and contact parent or guardian if the case is a child aged 5 years old or under. No further public health action is recommended until the results of further microbiological testing is available

2.3 Public health management of probable and confirmed cases of STEC (O157 and non-O157)

Cases may be defined as probable or confirmed STEC depending on their clinical, epidemiological and laboratory findings, as defined in Table 1. The public health management of probable and confirmed STEC O157 and O26 cases is described in Table 5.

Typically, the provisional identification of STEC O157 will be provided by the local diagnostic laboratory and later be confirmed by GBRU. Identification of STEC O26 is provided by GBRU based on a PCR assay typically available within 2 days of the *stx* and *eae* PCR profile. Because STEC O26 is associated with severe disease even in the absence of *stx2*, its identification should prompt public health actions commensurate those of STEC O157 or confirmed HUSEC.

The practical management of probable and confirmed cases is essentially the same for all higher risk strains including STEC O157, and the advice in tables 5 to 7 should be followed for cases and contacts. However, because confirmation of non-O157, non-O26 higher risk strain depends on the final *stx* subtyping results from WGS, the risk assessment – and thus the response – should be reviewed with each new result.

There may be circumstances that would suggest a lower risk strain needs to be managed as a higher risk strain, for example where WGS results indicate an unusually high number of cases or the HPT becomes aware of an outbreak.

Microbiological clearance and screening of contacts is not necessary for most cases from whom lower risk strains are isolated but this may be required in some situations as described above.

Very rarely, there may be more than one type of STEC present in a specimen (or a clearance specimen) which may differ in stx type and thus risk characterisation. Seek advice from GBRU colleagues in these cases.

Microbiological clearance and screening regimens for non-O157 higher risk strains are also different to those for STEC O157 because most local hospital laboratories cannot routinely isolate non-O157 STEC organisms.

Table 5. Public health management of probable and confirmed STEC cases

Case definition	Public health action
Probable • local O157 culture positive • probable HUS • symptomatic with epidemiological link • local stx PCR positive, local O157 culture negative, with bloody diarrhoea or hospitalization **Confirmed** • all cases with positive culture for STEC O157 • all cases with positive PCR for STEC O26 • STEC-related HUS	Full public health action Commence action on day of notification: • complete STEC enhanced surveillance questionnaire • ensure diagnostic laboratory initiates/completes diagnostic testing (see Section 1) and samples are sent to the GBRU as appropriate Control measures: • provide information and hygiene advice • advise exclusion and clearance sampes for case according to risk group • risk assess potential sources and consider further control measures as appropriate • identify any linked cases resulting from common exposure (define per Table 1) • identify and risk assess contacts for exclusion and/or microbiological screening Communication with relevant organisations or persons: • including environmental health officers (EHOs), GPs, child care settings and others

2.3.1 Exclusion and clearance of probable or confirmed cases of STEC (O157 and non-O157)

See Table 3. Groups at risk for ongoing transmission of gastrointestinal (GI) illness.

Exclusion and microbiological clearance are recommended for probable and confirmed STEC O157 or STEC O26 infections, and some other STEC cases with interim GBRU results, in accordance with recommendations and algorithms 1 to 3 of these guidelines. This includes PCR positive cases with bloody diarrhoea or hospitalization identified in Stage 1, for whom exclusion until 48 hours symptom free and possible clearance (depending on risk group membership) are recommended (see Stage 1 Algorithm).

For most cases from whom lower risk strains are isolated, microbiological clearance and screening of contacts is not necessary.

Table 6. Exclusion and microbiological clearance procedures for cases of STEC O157 infection and recommended non-O157 strains (guided by algorithms 1 to 3)

Risk group	Symptomatic	Recovered or asymptomatic for ≥48 hours
Case not in a risk group	Provide personal hygiene advice. Exclude until 48 hours symptom free. No microbiological clearance required.	No exclusion or microbiological clearance required
Case in risk group A, C or D	Provide personal hygiene advice. Exclude until microbiological clearance completed Arrange microbiological clearance Two consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours.	Provide personal hygiene advice Exclude and arrange microbiological clearance Two consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours. Review risk assessment to determine whether restriction or redeployment may be appropriate whilst awaiting results of microbiological testing (see below). If not appropriate, exclude case until microbiological clearance completed.
Case in risk group B	Provide personal hygiene advice. Exclude until microbiological clearance completed. Arrange microbiological clearance Two consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours.	Provide personal hygiene advice. Exclude until microbiological clearance completed. Arrange microbiological clearance. Two consecutive negative faecal samples taken ≥24 hours apart, once case is symptom free ≥48 hours. Review risk assessment to determine whether a supervised return to childcare settings may be appropriate whilst waiting for results

Table 6A. Demonstration of microbiological clearance for cases

Category	Demonstration of microbiological clearance
STEC O157	Where the diagnostic laboratory uses *stx* PCR, clearance may be conducted via PCR methods: • if the case is *stx* PCR negative on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required • if the case is *stx* PCR positive, local culture should be conducted and if negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required Where the diagnostic laboratory does not use *stx* PCR testing, clearance should be conducted via culture methods: • if the case is culture negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required
STEC Non-O157 (when recommended)	Where the diagnostic laboratory uses *stx* PCR, clearance may be conducted via PCR methods: 1. If the case is *stx* PCR negative on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required. 2. If the case is *stx* PCR positive, 2 approaches are possible: a) Continue *stx* PCR testing at locally agreed intervals until 2 consecutive samples are PCR negative. If PCR remains positive after 4 weeks of testing, consider sending a faecal sample to GBRU to see if STEC can still be isolated. b) Or submit faecal specimens to GBRU and if the case is found to be culture negative for non-O157 STEC on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required. Where the diagnostic laboratory does not use *stx* PCR testing, clearance should be conducted via culture methods: • samples should be submitted to GBRU, and • if the case is found to be culture negative for non-O157 STEC on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required

2.3.2 Local risk assessments for STEC cases

Local risk assessment for recovered or asymptomatic cases in groups A, C, and D

Results of the local risk assessment may determine whether restriction or redeployment within occupational settings is appropriate for cases in risk groups A, C, and D whilst awaiting microbiological clearance.

This may be guided by the duration and nature of symptoms, evidence of secondary transmission and an assessment of personal hygiene standards and facilities. This may include, for example, restriction of duties to exclude food handling or preparation or assistance with toileting of children but may facilitate redeployment to other duties. Such decisions should be made by HPTs in conjunction with relevant organisations, such as EH departments and following thorough discussion with the case and their responsible line manager. All cases should be excluded from all duties until symptom free for 48 hours or more. Risk assessments should be regularly reviewed.

Local risk assessment for asymptomatic or recovered cases in risk group B with prolonged shedding of STEC

General considerations are:

- HUS is associated with severe clinical outcomes (including fatalities)
- the infecting dose of STEC is low (several orders of magnitude lower than for *Salmonella*)
- children 5 years and under can shed STEC in faeces for 30 to 40 days, although the reported range of shedding duration is broad (6 to 16). Younger children may shed for longer than older children (6)

Transmission in childcare settings, including from asymptomatic children, is documented (although the degree of risk from asymptomatic children is not as well quantified) (8, 10 to 12).

Hence, for cases still shedding beyond 4 weeks, a risk assessment is recommended, including**:**

Age of the child and assessment of personal hygiene standards

Younger children may shed for longer than older children.

Conversely, if a child is an infant, it may be easier to ensure good hygiene at nappy changes, compared to a toddler who is toileting themselves.

An older supervised 4 year old may have good hand hygiene.

Assessment of facilities

Is it possible to provide supervised toileting and handwashing in childcare settings? Or can one staff member supervise or change the child's nappies or supervise handwashing after toilet use? Is there one toilet they can use?

Consider infection control procedures and environmental health assessment, in discussion with the school or nursery.

Virulence profile

The stx2a/stx2d profile has the highest risk of HUS. Thus, for cases with stx2a/stx2d, it is advisable to continue exclusion and await clearance. For other strains, provided the child did not have HUS, it may be possible to allow early supervised return at 4 weeks, provided the risk assessment supports this.

Evidence of any local transmission

Are there any other children in the childcare setting with diarrhoea or HUS? Have family members of the index case also been unwell? This may imply infection with a more transmissible strain.

The suggested risk assessment proforma in Appendix 2 of this guidance may be helpful in summarising these considerations.

After the initial risk assessment, a plan should be made for ongoing risk assessments. If the child is allowed back into the childcare setting, perform ongoing surveillance for the following 4 weeks and ensure symptomatic children are excluded. Testing of symptomatic children should be guided by the ongoing risk assessment, and is generally encouraged.

Review the frequency of microbiological testing for children who are excluded with prolonged shedding. Consider having weekly tests, rather than an increased frequency, which may increase anxiety in the family.

If a test is negative, then a subsequent one can be done 48 hours later.

Convene a multidisciplinary team to assist in the risk assessment. These teams should ideally include HPTs in conjunction with relevant stakeholders, such as public health microbiologists, infectious disease physicians or NIS experts and EH departments, directors of public health, and nursery or school representatives. A visit to the nursery by environmental health may be useful in assessing whether risks can be mitigated.

Results from these risk assessments should inform discussion with parents or guardians and childcare managers to ensure the public health benefit of continued exclusion is balanced against any potential harm from prolonged periods of exclusion. Risk assessments should be regularly reviewed and a plan agreed for the next assessment.

If the child is still colonised after 3 months, then consider any additional measures that can be used so that the child could return to school or nursery.

Cases with prolonged shedding should be communicated to the GBRU via the vtec@phe.gov.uk inbox in order to assist surveillance and provide an evidence base for action.

2.4 Public health management of CONTACTS of STEC cases (O157 and non-O157)

See Table 2. Definitions of contacts of a case of STEC infection.

See Table 3. Groups at risk for ongoing transmission of gastrointestinal (GI) illness.

It is important to remember that a symptomatic contact (recovered or not) with an epi link to a case is a probable case and may be the index case in a household – review Algorithm 1 and ensure that a diagnostic sample has been taken from the contact. If the case required a questionnaire, please ensure that the symptomatic contact also has a questionnaire completed

Exclusion and microbiological screening may be required for contacts of probable and confirmed STEC infections. This should be based on the findings of the initial risk assessment following notification of a probable or confirmed case and results of microbiological investigations.

The specific recommendations for exclusion and screening for contacts of cases are based on the available evidence of secondary transmission, carriage, groups at risk of severe disease and outbreak potential. Diagnostic criteria for demonstrating microbiological criteria for contacts of STEC O157, O26, and some non-O157 STEC cases with interim results (as guided by algorithms 1 to 3) are summarised below.

Table 7. Exclusion and microbiological screening for contacts of probable or confirmed cases of STEC O157, non-O157 HUSEC and other higher-risk strains including STEC O26

Contact type	Symptomatic	Recovered or no symptoms ≥48 hours
Contact not in a risk group	Provide personal hygiene advice. Manage as a probable case.	No public health action required.
Contact in risk group A, C or D	Provide personal hygiene advice. Manage as a probable case.	Provide personal hygiene advice. Exclusion and microbiological clearance are not routinely recommended (perform risk assessment for contacts in group A unable to perform adequate personal hygiene).
Contact in risk group B	Provide personal hygiene advice. Manage as a probable case.	Provide personal hygiene advice. Exclude and undertake microbiological screening for STEC infection. Single negative PCR sample or 2 consecutive faecal culture samples taken ≥24 hours apart: see Table 7A 'Demonstration of microbiological screening (contacts)' Undertake a risk assessment to determine if a return to school or other childcare setting is possible whilst waiting for results. This may include: • reinforcing supervised hand washing by childcare staff • where there is no ongoing contact with the index case • where contact with the index case is restricted and good personal hygiene can be maintained by the case (for example, separate bathroom or toilet facilities, no food preparation or handling by the index case)
Household of HUS case	In addition to the above risk group considerations, all household contacts of a case of HUS could be offered screening to identify and characterise the organism and guide public health management. Any contacts who test positive should be managed as cases.	

Table 7A. Demonstration of microbiological clearance for contacts

Category	Demonstration of microbiological clearance:
STEC O157	Where the diagnostic laboratory uses PCR for *stx* gene detection, screening may be conducted via PCR methods: • PCR is considered to have very high sensitivity. If the contact is found to be PCR negative on a single sample, no further microbiological testing is required • if the contact is PCR positive, local culture should be conducted and any isolate should be submitted to GBRU for further testing. • if local culture is negative, it is probable that the contact was infected but that the STEC is no longer viable or is present in very low numbers. HPTs may wish to discuss further testing with GBRU Where the diagnostic laboratory does not use PCR testing, screening should be conducted via culture methods: • if the contact is culture negative for STEC O157 on 2 consecutive samples taken at least 24 hours apart, no further microbiological testing is required
STEC non-O157 (where applicable)	Contacts may be considered to have demonstrated microbiological screening via the following diagnostic laboratory methods: Where the diagnostic laboratory uses PCR for *stx* gene detection, screening may be conducted via PCR methods: • PCR is very sensitive. If the contact is found to be PCR negative on a single sample, no further microbiological testing is required • If the contact is PCR positive, local culture should be conducted and if negative for O157, the faecal sample should be submitted to GBRU for further testing Where the diagnostic laboratory does not use PCR testing, screening should be conducted at GBRU: • if the contact is PCR negative at GBRU on a single sample, no further microbiological testing is required. If the PCR is positive, then await culture result. If the contact is negative on 2 consecutive culture samples taken at least 24 hours apart then no further microbiological testing is required

2.4.1 Recovered contacts

Recovered (that is, 48 or more hours without symptoms) contacts in risk groups A, C, and D

For contacts who are in risk groups A, C, or D who have been asymptomatic for 48 hours or more, exclusion and microbiological clearance are not routinely recommended. In an outbreak setting, microbiological screening of individuals might be undertaken to aid epidemiological investigation. In addition, for contacts in risk group A who are unable to perform adequate personal hygiene, a risk assessment should be completed to assess the need for exclusion and/or microbiological screening.

Recovered (48 or more hours without symptoms) contacts in risk group B

Microbiological screening of contacts in risk group B should commence once the index case is symptom free. In instances where contacts do not have ongoing contact with the index case, screening may commence immediately.

For cases with ongoing symptoms or prolonged excretion of STEC, a risk assessment may be conducted to agree the timing of when to commence contact screening as there may be continued exposure within the setting. This will involve assessment of likely compliance with personal hygiene measures and infection control in the home, access to use of separate bathroom or toilet facilities and restricting involvement in food preparation or handling by the index case.

For contacts in risk group B (particularly where the case is also in risk group B), minimising the risk of transmission is challenging. Stringent personal hygiene and infection control should be in place for all cases and contacts in these risk groups including the supervision of their toileting and hand hygiene. Where there is continual contact between cases and contacts in risk group B, the screening of contacts should not start until the case has been symptom free for at least 48 hours, Should the case become symptomatic again before their clearance has been completed, then risk group B contact screening will need to recommence once the case has become symptom free again for at least 48 hours.

2.4.2 Use of contact screening to identify the causative organism for HUS

For cases of HUS diagnosed clinically without full microbiological characterisation, alongside faecal testing of the symptomatic case, testing of household members is advised, in an effort to identify and characterise the organism and guide public health management.

Detecting the organism in an infected household contact’s stool can help reach a diagnosis by proxy for the case and guide further investigations and management. This may also help in identifying sources of transmission within the household and contain further person-to-person transmission. Finally, it can help confirm the diagnosis of STEC-associated HUS and avoid unnecessary treatment for atypical HUS.

The use of contact screening in this context is distinct from the recommended exclusion and screening of contacts in risk groups described in Table 7. Household contacts providing a specimen to aid in the investigation of HUS cases would not be expected to undertake exclusion while their results are pending, unless indicated for another reason (such as symptoms or membership of a risk group).

In some circumstances, tesing household members of HUS cases where STEC is already characterised may help with public health management and risk assessment of settings.

3. Outbreaks and clusters

3.1 Management of outbreaks and clusters

Outbreaks of STEC should be managed in accordance with agreed national and local outbreak plans and memorandums of understanding. The UKHSA national outbreak plan can be found online.

Suspected clusters or outbreaks should be notified promptly to the relevant FES team, national GI team, and partner organisations such as local NHS, EH departments and Local Authority Public Health teams. If potential exposures may have occurred in another HPT catchment, the relevant HPTs should be notified promptly.

HPTs and relevant partners should maintain a low threshold for establishing an outbreak control team (OCT) or incident management team (IMT) if a cluster or outbreak is suspected to facilitate identification and control of potential sources and implement control measures to prevent onward transmission.

Food and water contamination are well recognised and documented sources of STEC outbreaks. If food or water is the suspected source or vehicle and testing of food or water samples is required, HPTs can contact their local food, water and environment microbiology laboratories for advice on sampling. Special consideration may be required for outbreaks in settings where behaviour may increase the risk of spread of infection and the risk of severe infection in risk groups is increased.

3.1.1 Outbreaks associated with open farms

HPTs may consider the following when investigating and managing linked cases associated with an open farm:

Key partners may include the Local Authority Environmental Health teams, HSE, DEFRA, APHA, FSA and other UKHSA divisions (such as Regional Microbiology, FES, GBRU, I) and Communications teams.

HPTs or outbreak control teams (OCT) should work with enforcement agencies to facilitate business owners to protect the public's health and reduce onward transmission amongst visitors and staff.

Restriction of public access to animals, animal faecal matter and surfaces contaminated with animal faecal matter should be considered, including the potential for farm closure.
Sampling of potential sources may include animal faeces, manure, animal contact surfaces, water (particularly if there is potential for livestock contamination of private water supplies), fore-

stream milk, primary filters or washings and raw milk on dairy farms where raw milk may have been consumed.

Business operators should be directed to Access to Farms Partnership industry code of practice on preventing or controlling ill health from animal contact at visitor attractions (17), which includes advice on:

- premises layout and routes
- animal contact areas and livestock management
- eating areas
- play areas
- washing facilities
- visitor information and signage
- staff training and visitor supervision
- manure and compost heaps

Information on avoiding ill health when visiting open farms should be accessible to all visitors. An information leaflet Avoiding infection on farm visits: advice for the public is available online.

3.1.2 Outbreaks associated with nurseries, primary schools and other childcare settings

HPTs may consider the following when investigating and managing linked cases associated with a nursery, primary school or other childcare setting:

1. Work with enforcement agencies to facilitate early engagement with the manager or head teacher, key staff and parents which is important in ensuring cooperation and managing concern.

2. Other key partners may include the Local Authority (particularly the Education and Early Years teams and Environmental Health teams), other UKHSA divisions (such as Regional Microbiology, FES and GBRU) and communications teams. Local Primary Care and Acute NHS Trust teams may also be included due to the increased risk of severe infection in younger children attending these settings.

3. Links between children and/or staff within and outside the institution should be investigated to develop hypotheses about the source of infection (for example, common toileting facilities, common food source, school trips, after school clubs, social networks and so on). Mixing patterns, sharing of toys or play areas and the physical layout of the institution should also be assessed to determine potential routes for person-to-person transmission.

4. Cases and contacts in risk group B (children aged 5 years old and under attending childcare settings) should be excluded and microbiological testing or screening arranged as detailed in Sections 2 and 3 of this guidance. Additional testing and exclusion of older children and staff members will be determined by the OCT but may be implemented if a risk assessment suggests risk of ongoing environmental or person-to-person transmission.

5. Closure of all or part of the institution may be recommended by the OCT.

6. Information on hygiene measures within the institution and within the home should be provided to staff and parents to reduce onward transmission.

7. Communications should be agreed to provide advice and minimise concern amongst parents or families. This may be of particular importance in situations where children experience prolonged shedding STEC, requiring an extended period of exclusion from the childcare setting.

Appendix A. Supporting documents

Appendix A1. Table of GBRU in-house PCR results

GBRU – STEC isolated (STEC PCR:+ culture:+)

Receipt date	Sample date	Report date	Foreign travel	Organism identified	Sero type	Clonal complex	ST	EAE	STX1	STX2	AggR	STX subtype	SNP address
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				+	+	_			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				+	+	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				+	-	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				-	+	-			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				-	+	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC isolated (STEC PCR:+ culture:+)				-	-	+			

GBRU – STX genes detected (STEC PCR:+ culture

Receipt date	Sample date	Report date	Foreign travel	Organism identified	Sero type	Clonal complex	ST	EAE	STX1	STX2	AggR	STX subtype	SNP address
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				+	+	_			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				+	+	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				+	-	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				-	+	_			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				-	+	+			
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STX genes detected (STEC PCR:+ culture)				-	-	+			

GBRU – STEC NOT isolated (STEC PCR:- culture)

Receipt date	Sample date	Report date	Foreign travel	Organism identified	Sero type	Clonal complex	ST	EAE	STX1	STX2	AggR	STX subtype	SNP address
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		STEC NOT isolated (STEC PCR:- culture)									

GBRU – serogroup or serotype result

Receipt date	Sample date	Report date	Foreign travel	Organism identified	Sero type	Clonal complex	ST	EAE	STX1	STX2	AggR	STX subtype	SNP address
yyyy-mm-dd	yyyy-mm-dd	yyyy-mm-dd		*Escherichia coli*	O26:H11	CC21	29	+	+	-		1a	

Appendix A2. STEC risk assessment proforma

Case name		HPZ number		Date	
Clinical picture					
Date of onset, symptoms (bloody diarrhoea) Date symptoms ceased or ongoing					
Key risks					
Case (Risk group) A. Inadequate hygiene B. Children 5 years and under C. Food handler D. Direct patient contact		**C** (Risk group) A. Inadequate hygiene B. Children 5 years and under C. Food handler D. Direct patient contact	1 2 3 4 5		
Employer, school or nursery		General hygiene standards, awareness and so on			
Hygiene standards and considerations					
Hygiene facilities in home – separation of bathroom and WC		Activities attending			
If child – nappies or toilet trained		Result of EH assessment (where undertaken)			
Decision					
Rational for decision and who involved in decision					
Assessor name		Signature		Date	

Appendix A3. STEC: PCR letter

Date

Our ref: HPZ

Private and confidential

Patient address

Dear,

Re: Recent laboratory result on your stool sample

The UK Health Security Agency (UKHSA) health protection team for insert name of HPT has been informed by the local laboratory that the results on a stool (faeces, poo) sample that you or your child submitted may be positive for bacteria called Shiga toxin-producing *Escherichia coli* (STEC).

STEC is a notifiable disease. Clinicians and laboratories are required to report any illness where the suspected cause is STEC to UKHSA. Our role is to try and identify the source if possible and give advice to help prevent the spread of infection to other people
The sample may have been sent to the UKHSA reference laboratory in London for further testing. If this was done the results should be available in several weeks and will be sent to the doctor who requested the sample.

In the meantime, please telephone us on Insert HPT name and contact number if:

- your symptoms included bloody diarrhoea

or:

- you attended hospital for your acute diarrhoeal illness

or:

- any other member of your household has experienced similar symptoms either 7 days before or 7 days after yours started

This will help us to gather more information on your illness and provide any relevant further advice.

Please read the accompanying leaflet which provides information about STEC and what actions you should now take, including information on how to prevent the spread of infection.

Kind regards,

Copy: Doctor

Appendix A4. Non-O157 STEC PCR leaflet

STEC (Shiga toxin-producing *Escherichia coli*)

An information leaflet for cases

Why you have been contacted

The UK Health Security Agency (UKHSA) insert team name health protection team is contacting you because the result of the stool (faeces, poo) sample submitted by you or your child is positive for a bacterium called Shiga toxin-producing *Escherichia coli* (STEC), sometimes known as VTEC.

The local laboratory test has detected genetic material (DNA) of STEC bacteria, and has confirmed that you are unlikely to have STEC O157, the most common strain of STEC in the UK which often causes more serious illness, It is likely that your infection is caused by another strain of STEC that usually causes mild illness.

Many NHS laboratories send samples to the UKHSA reference laboratory in London for further tests to identify the exact strain. If further testing has been done, then in a few weeks the result will be sent to the doctor who arranged for your sample and the health protection team or Environmental Health team may contact you for further information.

In the meantime, because some strains can cause serious illness and can be passed from person to person, we are contacting you to:

- identify potential sources of the infection
- provide some information on the infection and how you can prevent the spread of infection to others

What happens now

Please read the leaflet. If you have any concerns or questions that are not answered after reading the rest of this leaflet please contact your local health protection team.

Symptoms

Most people get better within 5 to 7 days. Treatment involves drinking plenty of fluids as vomiting and diarrhoea can lead to dehydration. Antibiotics should not be used as there is no evidence that they are helpful to treat STEC infections and they may increase the risk of complications.

Rarely, symptoms may be severe or even life-threatening causing haemolytic uraemic syndrome (HUS) which may occur up to 2 weeks after the start of the diarrhoea. If your symptoms do not go away or you develop easy bruising, feel you are passing less urine than usual or your urine is pink or brown in colour, please urgently seek medical advice as these symptoms could indicate the start of HUS and you may need further investigation from the NHS.

Staying away from work or school and nursery

You should stay away from work, school or nursery until you have stopped having symptoms for at least 48 hours to avoid passing it on to others.

For some people, this time may be longer and further samples may be needed because of the higher chance of spreading the infection to others or spreading it to people who may be more likely to develop severe illness. This may include:

- those that need help with their own personal hygiene at home, work or school
- children aged 5 years and under, particularly those attending nursery or pre-school groups
- those that prepare or serve unwrapped food that is not heated further
- healthcare workers with direct contact with highly susceptible patients for whom an infection like STEC could have serious consequences

Children aged 5 years and under (up to sixth birthday)

Although rare, the risk of HUS is highest in children aged 5 years and under. Some children aged 5 years and under have also been shown to continue to pass STEC in their stool for longer than adults, sometimes for many weeks or even months.

For these reasons, children aged 5 years and under may need to stay away (be excluded) from childcare settings until their stool samples are clear of the infection. If there are other children aged 5 years and under in the household, they may also be excluded, whether they have symptoms or not, until stool samples show that they have not picked up the infection.

Your local UKHSA Health Protection or Environmental Health Officers will be in contact to advise you if exclusion is needed for you and/or your contacts. They will provide you with information on this clearance process and aim to support you to get you or your child back to normal activities as quickly as possible.

Please read the rest of this leaflet and in particular follow the advice on ‘How can I prevent others from becoming ill?’ to minimise passing the infection on to others.

General information on STEC

Explanation of STEC

STEC (Shiga toxin-producing *Escherichia coli)* can cause illness ranging from mild diarrhoea to life threatening conditions. STEC O157 is the most common type in the UK and in a small number of people can cause very serious illness called haemolytic uraemic syndrome (HUS). The risk of HUS is highest in children aged 5 years and under.

We know that STEC is very infectious and can be easily passed to others. It has also been the cause of several outbreaks following eating infected food, contact with infected people and touching infected animals or their faeces.

In some European countries, other types of STEC are the cause of serious illness and outbreaks.

How people get infected

You may become infected with STEC in a variety of ways:

- eating infected or contaminated food that has not been cooked all the way through, particularly minced meat products such as burgers and sausages, or salad items that have not been washed properly
- handling or preparation of food contaminated with soil, for example, potatoes and leeks where the soil has not been washed away
- drinking infected or contaminated water such as from streams, rivers and lakes and so on which may contain animal faeces
- close contact with animals, particularly cattle, sheep and goats – animal saliva may be infected because of the way animals clean themselves
- direct contact with animal faeces on the animal itself, in their pen or on the floor
- contact with an infected person, particularly if you don't wash your hands thoroughly after using the toilet or before handling food

Symptoms

It usually takes between 2 and 4 days from being infected with STEC to develop symptoms which may be:

- no symptoms
- very mild diarrhea
- stomach pain
- vomiting
- fever
- severe diarrhoea with blood
- passing less urine than normal
- haemolytic uraemic syndrome (HUS)

How to prevent others from becoming ill

Normal cooking temperatures kill STEC and it can be easily washed off your hands. For extra reassurance, you can use antibacterial gels or wipes after washing your hands with soap and water.

Important steps you can take include:

- wash hands thoroughly with liquid soap and running water after using the toilet (or helping others including changing nappies), handling raw meat, before meals and after contact with animals. If you have false nails, pay particular attention to cleaning these thoroughly
- clean hard surfaces including toilet bowls, flush handles, taps and hand basins regularly with hot soapy water followed by a disinfectant or sanitiser
- wash dirty clothes, bedding and towels on the hottest wash cycle possible and do not share towels or face flannels with someone who is infected

- clean animal faeces from footwear or buggy wheels after visits to animal attractions and wash your hands after doing so
- stay away from work, school or nursery until 48 hours after you've stopped vomiting or having diarrhoea and comply with any additional exclusions recommended by the environmental health or health protection teams

Further information about STEC

Further information relating to STEC can be found on the following websites:

- NHS Choices
- UK Health Security Agency
- The Haemolytic Uraemic Syndrome Help (HUSH) support group

Appendix A5. STEC O157 leaflet

STEC O157 (Shiga toxin-producing *Escherichia coli*)

An information leaflet for cases

Why you have been contacted

The UK Health Security Agency (UKHSA) insert team name health protection team is contacting you because the result of the stool (faeces, poo) sample submitted by you or your child is positive for a bacterium called Shiga toxin-producing *Escherichia coli* (STEC) O157, also known as *E.coli* O157. *E.coli* O157 is the most common strain of STEC found in the UK.

The local laboratory has sent your sample to the UKHSA reference laboratory in London for further investigations and the final results may not be available for several weeks.

In the meantime, because *E.coli* O157 can cause serious illness and can be passed from person to person, we are contacting you to:

- identify potential sources of the infection
- provide some information on the infection and how you can prevent the spread of infection to others

What happens next

Along with our colleagues in Environmental Health, we will complete a questionnaire with you to help identify the potential sources of your infection and risk to any of your contacts. This will include:

- the activities you have done and food you have eaten in the 7 days before your symptoms started
- information on you and your household or close contacts
- providing information on the infection and how you can prevent the spread of infection to others

Your personal identifiable information will be held confidentially and only shared with colleagues directly involved in managing this infection in accordance with General Data Protection Regulations (GDPR) (EU) 2016/679.

Symptoms

Most people get better within 5 to 7 days. Treatment involves drinking plenty of fluids as vomiting and diarrhoea can lead to dehydration. Antibiotics should not be used as there is no

evidence that they are helpful to treat STEC infections and they may increase the risk of complications.

Rarely, symptoms may be severe or even life-threatening causing haemolytic uraemic syndrome (HUS) which may occur up to 2 weeks after the start of the diarrhoea. If your symptoms do not go away or you develop easy bruising, feel you are passing less urine than usual or your urine is pink/brown in colour please urgently seek medical advice as these symptoms could indicate the start of HUS and you may need further tests.

Staying away from work or school or nursery

You should stay away from work, school or nursery until you have stopped having symptoms for at least 48 hours to avoid passing it on to others.

For some people, this time may be longer and further samples may be needed because of the higher chance of spreading the infection to others or spreading it to people who may be more likely to develop severe illness. This may include:

- those that need help with their own personal hygiene at home, work or school
- children aged 5 years and under, particularly those attending nursery or pre-school groups
- those that prepare or serve unwrapped food that is not heated further
- healthcare workers with direct contact with highly susceptible patients for whom an infection like STEC could have serious consequences

Children aged 5 years and under (up to sixth birthday)

Although rare, the risk of HUS is highest in children aged 5 years and under. Some children aged 5 years and under have also been shown to continue to pass STEC in their stool for longer than adults, sometimes for many weeks or even months.

For these reasons, children aged 5 years and under may need to stay away (be excluded) from childcare settings until their stool samples are clear of the infection. If there are other children aged 5 years and under in the household, they may also be excluded, whether they have symptoms or not, until stool samples show that they have not picked up the infection.

Your local UKHSA Health Protection or Environmental Health Officers will be in contact to advise you if exclusion is needed for you and/or your contacts. They will provide you with information on this clearance process and aim to support you to get you or your child back to normal activities as quickly as possible.

Please read the rest of this leaflet and in particular follow the advice on ‘How to prevent others from becoming ill’ to minimise passing the infection on to others.

General information on STEC

What STEC is

STEC (Shiga toxin-producing *Escherichia coli)* can cause illness ranging from mild diarrhoea to life threatening conditions. STEC O157 is the most common type in the UK and in a small number of people can cause very serious illness called haemolytic uraemic syndrome (HUS). The risk of HUS is highest in children aged 5 years and under.

We know that STEC is very infectious and can be easily passed to others. It has also been the cause of several outbreaks following eating infected food, contact with infected people and touching infected animals or their faeces.

In some European countries, other types of STEC are the cause of serious illness and outbreaks.

How people get infected

You may become infected with STEC in a variety of ways:

- eating infected or contaminated food that has not been cooked all the way through, particularly minced meat products such as burgers and sausages, or salad items that have not been washed properly
- handling or preparation of food contaminated with soil, for example, potatoes and leeks where the soil has not been washed away
- drinking infected or contaminated water such as from streams, rivers and lakes and so on, which may contain animal faeces
- close contact with animals, particularly cattle, sheep and goats – animal saliva may be infected because of the way animals clean themselves
- direct contact with animal faeces on the animal itself, in their pen or on the floor
- contact with an infected person, particularly if you don’t wash your hands thoroughly after using the toilet or before handling food

Symptoms

It usually takes between 2 and 4 days from being infected with STEC to develop symptoms, which may include:

- no symptoms
- very mild diarrhea
- stomach pain
- vomiting
- fever
- severe diarrhoea with blood
- passing less urine than normal
- haemolytic uraemic syndrome (HUS)

How to prevent others from becoming ill

Normal cooking temperatures kill STEC and it can be easily washed off your hands. For extra reassurance, you can use antibacterial gels or wipes after washing your hands with soap and water.

The main steps you can take include:

- wash hands thoroughly with liquid soap and running water after using the toilet (or helping others including changing nappies), handling raw meat, before meals and after contact with animals. If you have false nails, pay particular attention to cleaning these thoroughly
- clean hard surfaces including toilet bowls, flush handles, taps and hand basins regularly with hot soapy water followed by a disinfectant or sanitiser
- wash dirty clothes, bedding and towels on the hottest wash cycle possible and do not share towels or face flannels with someone who is infected
- clean animal faeces from footwear or buggy wheels after visits to animal attractions and wash your hands after doing so
- stay away from work, school or nursery until 48 hours after you've stopped vomiting or having diarrhoea and comply with any additional exclusions recommended by the environmental health or health protection teams

More information about STEC

More about STEC can be found on the following websites:

- NHS Choices
- UK Health Security Agency
- The Haemolytic uraemic syndrome Help (HUSH) support group

Appendix A6. Guidance development

STEC Working Group for Guidance Development 2021

Nachi Arunachalam, Sooria Balasegaram, Lisa Byrne, Girija Dabke, Trent Herdman, Gauri Godbole, Claire Jenkins, Rohini Manuel, Qanita Vahora, Gemma Ward.

STEC Working Group for Guidance Evaluation 2019 to 2021

Sooria Balasegaram, Saira Butt, Lisa Byrne, Kevin Carroll, Trent Herdman, Gauri Godbole, Claire Jenkins, Piers Mook, Qanita Vahora, Bhavita Vishram, Gemma Ward.

STEC Working Group 2018

Bob Adak, Neil Anstey, Sooria Balasegaram, Lisa Byrne, Kevin Carroll, Girija Dabke, Richard Elson, Gauri Godbole, Lisa Harvey-Vince, Jeremy Hawker, Claire Jenkins, Trish Mannes (Chair), Rohini Manuel, Amy Mikhail, Kitty Mohan, Karthik Paranthaman, Samia Latif, Gemma Ward, Deborah Wilson.

Lead Authors: Sooria Balasegaram, Kevin Carroll, Lisa Harvey-Vince, Gemma Ward.

Acknowledgements

PHE and UKHSA Gastrointestinal Infections Leads Network.
All those who commented on the guidelines.

Appendix B. Background information

Background

Shiga toxin-producing *Escherichia coli* (STEC) are pathogenic strains of *E. coli*, characterised by the production of Shiga toxins. The spectrum of symptoms of STEC infection is broad, ranging from asymptomatic carriage through mild gastrointestinal symptoms to severe illness presenting with bloody diarrhoea or the development of haemolytic uraemic syndrome (HUS).

E. coli O157 is the most commonly identified serogroup worldwide, and the basis for most evidence concerning STEC (18). However, non-O157 STEC strains are increasingly recognised as the cause of human illness and outbreaks. For every STEC O157 clinical isolate, there are estimated to be 4 to 7 non-O157 STEC isolates, each possessing a combination of stx1 and stx2 subtypes and virulence factors (eae/aggR) that may give rise to illness ranging from mild symptoms to HUS.

This appendix describes the epidemiology and clinical burden of disease associated with O157 and non-O157 STEC infections.

Clinical features

Incubation period

The incubation period for STEC O157 has a reported range from 6 hours to 10 days, although 2 to 4 days is the most common (19 to 23). The incubation period for other serogroups is less well characterized, but likely to be similar (however, a single study of 91 cases in an O104 outbreak reported a median incubation period of 8 days, interquartile range 6 to 10) (19). The incubation period may depend on the number of organisms ingested.

Period of shedding

The period of shedding of STEC organisms is considered to be up to around 7 days in adults (19). In children, prolonged shedding may occur. In a UK study of confirmed cases of STEC in children aged ≤5 years attending childcare facilities, the average duration of shedding was 31 days (6), with other studies reporting similar results, of 29 days (range 11 to 57 days) (9). In the study of children attending childcare facilities in the UK, 24% were found to be continuing to shed for ≥6 weeks (6). The duration of shedding may be affected by age and severity of illness and may differ between cases of STEC O157 and non-O157 STEC serotypes.

Evidence regarding the infectious dose, transmissibility and duration of shedding of STEC by human cases has been derived principally from cases of STEC O157. While there is less evidence regarding transmission and duration of shedding associated with non-O157 STEC infections, there is consensus that prolonged shedding in young children is common, with a

median duration of about 30 to 40 days (with younger patients shedding for longer), but the range is broad. There does not appear to be any differences related to sex, severity of disease, or stx subtype in the median duration of shedding (15).

In outbreaks, secondary case rates between 7 and 21% for STEC O157 have been reported; similar transmission rates have been seen in outbreaks associated with non-O157 STEC serogroups (15, 16). In households, the highest rates of transmission are generally seen when the sources are young children. The youngest children are also those at greatest risk of acquiring the infection in households (24).

Clinical presentation and sequelae

Infection with STEC may be asymptomatic or cause a spectrum of illness from mild non-bloody diarrhoea to bloody diarrhoea, haemolytic uraemic syndrome (HUS) and death.

In addition to non-bloody diarrhoea, symptoms of milder infection may include fever, abdominal pain or cramps and vomiting.

More severe symptoms may reflect haemorrhagic colitis, with patients developing bloody diarrhoea and severe abdominal pain. The GBRU surveillance data study (England and Wales) reported symptoms of bloody diarrhoea in 61% and abdominal pain in 79.2% of patients with STEC O157 infection (25). The illness is usually self-limiting with recovery in less than 10 days (19).

HUS is characterised by acute renal failure, thrombocytopenia and microangiopathic haemolytic anaemia. Up to 10% of STEC cases are estimated to develop HUS, although this may differ for cases of non-O157 STEC infection (19, 25).

Children aged less than 5 years of age (especially those between one and 4 years old) are at greatest risk of developing HUS, which usually occurs approximately one week after the onset of bloody diarrhoea (26, 27). Hospitalized patients aged over 60 are also at increased risk of HUS. The majority of patients recover from HUS, although around 50% may develop chronic renal complications (usually mild); mortality is estimated to be between 3 to 5% (19).

Use of antibiotics

The use of antibiotics to treat infection with STEC is not routinely recommended. A recently conducted meta-analysis identified that when considering only those studies with a low risk of bias and appropriate definition of HUS, a significant association was found between the use of antibiotics and the risk of developing HUS (28).

Determinants of virulence

Most strains of O157:H7 STEC are eae positive and possess stx2a/2c genotypes with or without stx1a. Non-O157 STEC serogroups are a heterogeneous group of organisms that can

cause a similar spectrum of illnesses to STEC O157. Over 100 serogroups have been documented in cause human illness, with the majority of reported cases associated with non-O157 STEC having diarrhoeal illness of short duration. However, several serogroups are regularly associated with more severe forms of human illness. In the USA, CDC data shows that 75 to 80% of reported and serogrouped non-O157 STEC isolates from humans with severe symptoms (including bloody diarrhoea and HUS) belong to serogroups O26, O45, O103, O111, O121, and O145 (17, 29, 30). Serotypes belonging to these serogroups possess combinations of Shiga toxin subtypes and other virulence factors that are associated with the development of HUS and bloody diarrhoea (31). Serogroup O26, in particular, has been recognised as an emerging cause of severe disease in England (32).

The potential of STEC organisms to cause severe disease relates to the expression of stx genes, which produce cytotoxic damage and inflammation, and genes that promote attachment and adherence to the gut mucosa (in particular eae, but also aggR and other genes) (33). The combination of Shiga toxin subtype stx2a and the virulence factor eae has the strongest association with toxicity; stx2d and stx2c are also associated with severe disease. Stx1, stx2b, stx2e, and stx2f are the least potent toxins. Stx2c has intermediate potency, but is 25 times less potent than stx2a. In 2011, a hybrid STEC strain (O104:H4, stx2a, aggR) emerged that caused a large Europe wide outbreak with a high incidence of HUS affecting mainly adults (34). This strain possesses an adherence factor aggR that is distinct from eae and significantly enhances the virulence of the strain. In England during 2014, an STEC strain (O55:H7, stx2a, eae) emerged that caused an outbreak in which 42% of cases developed HUS (35) and in France, an STEC serotype O80:H2 has become a significant problem, with 91% of cases developing HUS (36). The strains possessed combinations of stx2a, stx2c and stx2d with eae (37).

Significance for public health response

The significance of these findings for public health is that most STEC strains can cause diarrhoeal illnesses, and any organism producing Shiga toxin has the potential to cause HUS. However, most strains commonly causing severe illness in humans possess stx subtypes stx2a, stx2c or stx2d and eae or aggR virulence factors – collectively referred to in the current guidance as higher risk strains. This encompasses strains associated with HUS (HUSEC) and strains associated with severe illness other than HUS, such as bloody diarrhoea. In South East England, it is estimated that around 10% of successfully serotyped isolates belong to higher risk strains other than STEC O157. Public health actions should be prioritised to cases infected with O157 and higher risk non-O157 strains (including HUSEC) (31, 33).

Sources and transmission

STEC colonise the gastrointestinal tracts of farm animals, primarily cattle, usually without causing illness. Sheep, goats and deer are also significant reservoirs, with other wild and domestic animals including pigs, dogs, and birds also able to act as vectors of disease for both STEC O157 and non-O157 (38 to 41). In an ecological study of Germany, a positive association

was found for the incidence of 5 HUS-relevant STEC serogroups in paediatric patients (O26, O103, O111, O145, O157) and cattle density in the geographical area of residence (42).

Any food, water or environmental surface contaminated by the excreta of an animal or human case, including asymptomatic carriers, is a potential source of infection. The organism is highly virulent and the infectious dose is low, possibly less than 100 organisms (43), facilitating its potential to cause large outbreaks of human illness.

Food

Human infection with STEC is most commonly due to consumption of contaminated foods, particularly raw or undercooked ground meat products (19, 44). The surface of meat can be contaminated during slaughter and processing. When spread through the whole product, as in hamburgers and other ground meat products, this poses a particular risk if inadequately cooked. Unpasteurised or inadequately pasteurised milk also poses a risk from faecal contamination. Contamination of ready-to-eat foods, via cross-contamination from raw meat products, is an important cause of foodborne STEC infections. Food vehicles implicated in large-scale outbreaks worldwide include meat and dairy products (45 to 47), salad products such as lettuce (48), sprouted seeds, such as fenugreek (34, 49), raw fruits and vegetables and associated products such as apple juice (45).

Most large outbreaks associated with non-O157 STEC have been associated with contaminated food or water as the main vehicle of infection. An analysis of outbreaks in the USA found that of 38 single-aetiology outbreaks, 66% were caused by non-O157 and 84% and transmitted through food or person-to-person spread (50). Childcare centres were the most common setting for person-to-person spread. Person to person spread has been reported more often in association with non-O157 STEC infections compared to O157 (38).

Primary prevention of transmission via food products involves minimising contamination of animal carcasses during slaughter, good kitchen practices to avoid cross-contamination of raw and cooked foods, thorough cooking of meat products, pasteurisation of milk and dairy products and ensuring personal hygiene, most specifically thorough handwashing (43).

Water

Both surface water and private water supplies have the potential for contamination with STEC via animal excreta. Sporadic cases and outbreaks linked to waterborne sources have been documented worldwide. These have been associated with exposure to bacteria via swimming in lakes, pools and consumption of water from farm wells and private water supplies (45). There are fewer reports of water associated outbreaks (51, 52) caused by non-O157 STEC serogroups than for STEC O157. In the Republic of Ireland outbreaks caused by O26 STEC serotypes are regularly associated with private water sources (53, 54).

Livestock and farms

Due to the recognised reservoir of STEC amongst animals, especially ruminants, human infection may follow occupational or recreational exposure to animals, their excreta or the environment contaminated by them.

For A large-scale outbreak of E. coli O157 linked to an open farm in the UK in 2009 highlighted the importance of minimising or eliminating visitor contact with animal excreta and raising public awareness of the importance of hand hygiene during recreational farm visits (55). Cases of non-O157 STEC have also been associated with contact with farm animals (25). Visits to petting farms and agricultural fairs have also been implicated in outbreaks of STEC infection (45). Farm workers are also at risk of infection with STEC through occupational exposure.

There is little information about the transmission of non-O157 STEC infections related to animal contact. A meta-analysis has indicated that infections from undercooked or raw meat occur more often with O157 strains while non-O157 strains are more often associated with animal contact but only 6 out of 31 studies contained sufficient information to enable this comparison to be done (56).

Person-to-person spread

Transmission of STEC from person-to-person is via the faecal-oral route and is a recognised cause of outbreaks of STEC infection worldwide. A review of 90 outbreaks across 9 countries identified the most common mode of secondary transmission to be person-to-person spread within household settings (46%) (44).

The evidence for food handlers acting as the primary source of transmission within outbreaks in the UK is limited. A 2014 review of UK STEC O157 outbreaks between the 1980s and 2013 did not identify food handlers as the primary source of transmission in any of the included outbreaks (52).

For outbreaks with secondary transmission via person-to-person spread in nursery settings, higher rates of secondary cases were noted which are likely to reflect a combination of factors including prolonged shedding in this age group, poor/under-developed personal hygiene measures and immature immune systems in this age group (44). Other studies of sporadic cases of STEC infection have also identified contact with symptomatic young children (aged less than 5 years) as being a risk factor for transmission (57).

There have been numerous reports of outbreaks probably caused by person-to-person spread of non-O157 STEC in day-care (14 to 16, 24), schools and senior care facilities, and it appears that this form of spread might be a more common route for non-O157 STEC infections. Transmission by infected food handlers is a recognised risk and there are reports in the published literature. One outbreak was reported involving a prison and epidemiological investigations implicated an infected food handler, the outbreak was caused by STEC serogroup O45 (stx1) (58).

There were 341 probable cases during a large restaurant associated outbreak caused by O111 STEC in Oklahoma and epidemiological evidence suggested the outbreak resulted from cross-contamination of restaurant food from food preparation equipment or surfaces, or from an unidentified infected food handler (59). During the O104:H4 outbreak in Germany a cluster of 23 cases in a family party associated with a restaurant is postulated to have been caused by a food handler contaminating several food items from which the organism was isolated (60).

Epidemiology

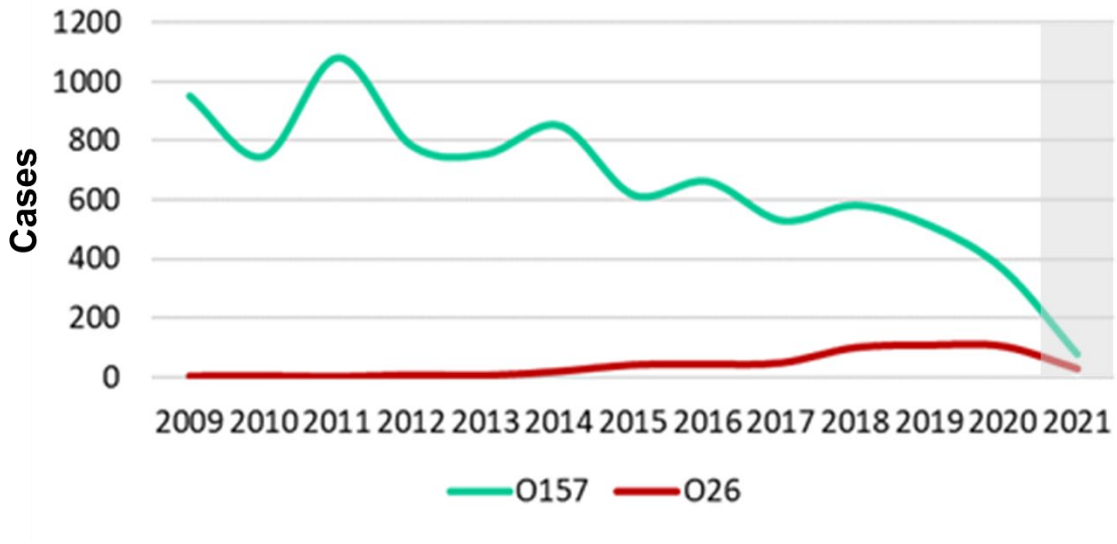
The accuracy of epidemiological surveillance depends upon recognition by diagnostic and reporting mechanisms. In England, all STEC infections are notifiable, but the ease with which pathogens can be isolated in diagnostic laboratories differs between O157 and non-O157 serogroups. E. coli O157 is the most common serogroup of STEC causing infections in the UK. It is also the most likely E.coli serogroup to cause bloody diarrhoea in the UK, and HUS worldwide (33). Whereas diagnostic laboratories can routinely identify cultured O157, non-O157 STEC cannot be easily distinguished from other E. coli by routine culture methods, so the reported incidence varies with laboratory practice, and true incidence of non-O157 STEC is not known.

Over recent years, many local diagnostic laboratories have implemented stx PCR testing of faecal specimens, enabling the preliminary identification of non-O157 STEC, with the potential for confirmation in the GBRU. This has led to a rapid increase in non-O157 STEC isolation, from 18 cases in 2011 to over 500 a year between 2018 and 2020 (25).

Confirmed human isolates of STEC O157 in England increased markedly from the late 1980s, peaking in the late 1990s. Between 2005 and 2015, between 630 and 1091 isolates of STEC O157 have been confirmed annually from human sources. From 2017, the incidence of STEC O157 has fallen further in England, with 532 cases in 2017 to 365 in 2020.

Meanwhile, detection of non-O157 serogroups has increased, driven in part by greater capacity to screen for stx genes by PCR in local diagnostic laboratories. The proportion of confirmed STEC isolates confirmed as non-O157 serogroups has risen in recent years, from 34% in 2018 to 39% in 2019 to 42% in 2020. In particular, identification of the most common non-O157 serogroup, STEC O26 has risen: from 48 in 2017 to 104 in 2020 (Figure 1).

Figure 1. Cases of STEC O157 and O26 in England, 2009 to 2021 (as of 24 June 2021)



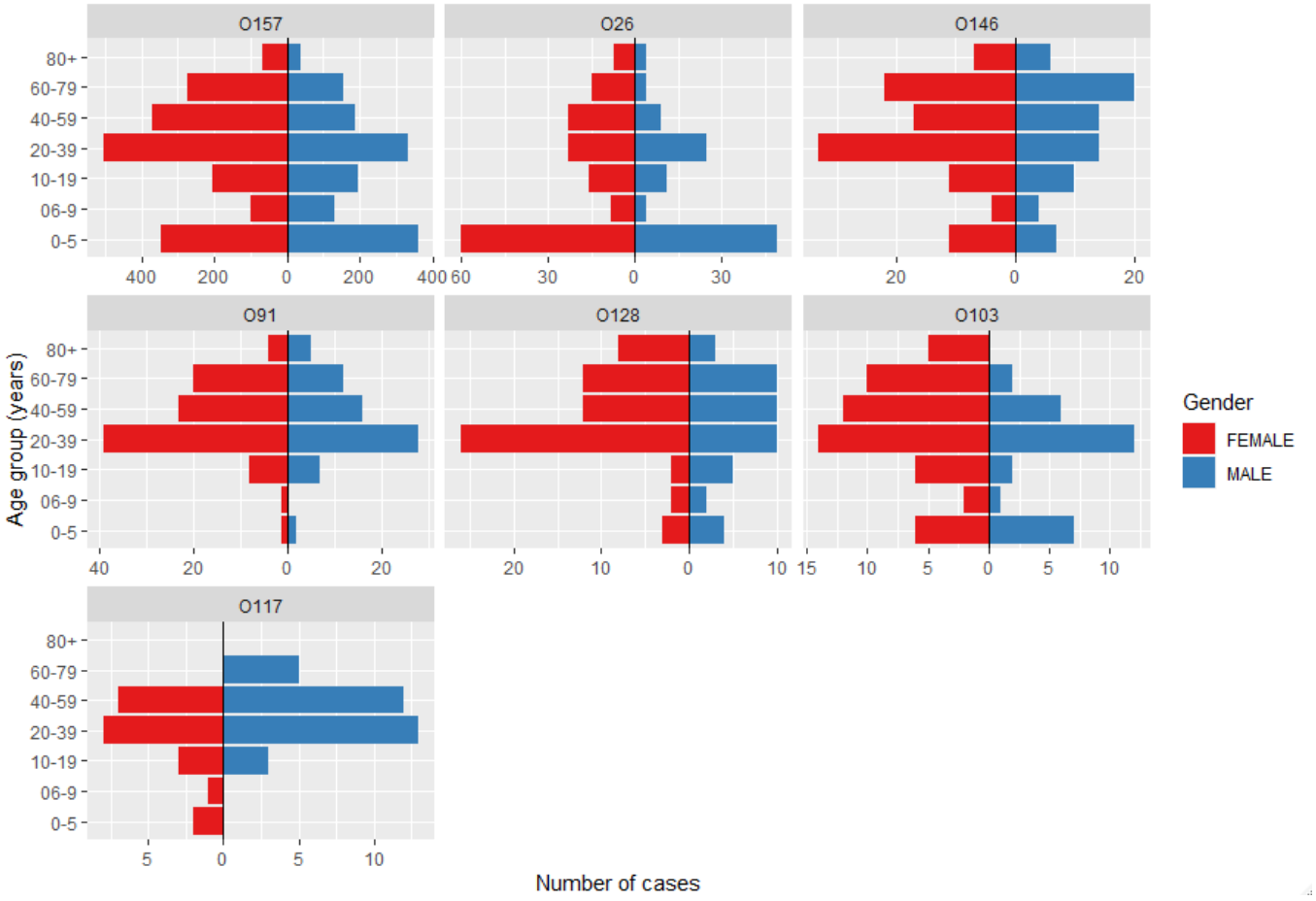
Seasonality of STEC O157 infections in England shows a peak in the third quarter with fewer infections in the first quarter. Non-O157 serogroups and PCR show some seasonality, though it is less marked (61).

Reported incidence of STEC O157 varies within England, with the highest rates occurring in the north and South West of England (62). Around 62% of cases are regarded as sporadic, 19% are identified as part of household clusters, and 19% are part of general outbreaks (PHE data). 21% of cases reported to national surveillance reported foreign travel between 2009 and 2015, although the numbers differ by phage type, with PT21/28 being the predominant indigenously acquired UK strain (63).

Children under 16 years old account for almost 50% of cases (64), and rates of infection are highest in children under 5 years with the peak incidence in the 1 to 4 age group (Figure 2) (32, 63). Some of this excess may reflect screening practices, as young children are routinely screened for STEC following a case in a household, whereas adult contacts may not be screened unless they are in a risk group. However, children 5 years and under are also more susceptible to clinical illness. Around a third (34%) of STEC O157 cases are hospitalised, with a median duration of 3 days (IQR 1 to 21 days) (63).

HUS occurs in up to 11% of STEC O157 cases, and 85% of patients with HUS are under 16 years of age (64). Progression to HUS is associated with being one to 4 years of age, being female, being infected with PT21/28 or PT2, receiving β-lactam antibiotics or presenting with vomiting or bloody diarrhoea. The chances are increased further when all of these factors are present (27).

Figure 2. Age-sex distribution of STEC cases in England 2014 to 2018 by serogroup (32)



Overall incidence of non-O157 STEC is difficult to estimate from routine surveillance, as practices for microbiological characterization differ by clinical and operational context. A recent study in the South East of England described all stx PCR-positive results from local diagnostic laboratories, and found an overall annual incidence rate of STEC infections (PCR or culture confirmed) of 5.8 cases per 100,000 population, with a ratio of STEC O157 to non-O157 STEC of 1 to 7 (61). These findings are comparable to a large prospective, population-based studies of infectious intestinal disease (IID) incidence and aetiology conducted in the UK in 2008 to 2009 (IID2), which also estimated a ratio of O157 to non-O157 STEC infections of 1 to 7 (65).

Recent analysis of virulence factors in non-O157 STEC supports the strategy for prioritizing cases with stx2 and eae genes while awaiting final characterization by the GBRU. Among confirmed cases of higher risk non-O157 STEC isolated by GBRU 2018 to 2020, 76% (287 of 380) had this profile on initial PCR testing – most of the remaining cases (91 of 93) were stx2 positive but eae negative, and likely possessed aggR or another attachment virulence factor. Conversely, 91% of confirmed lower risk STEC isolates (2,114 of 2,323) lacked this PCR profile.

The early identification of STEC infections associated with severe disease is enhanced further by increased emphasis on STEC O26. Among cases confirmed by GBRU 2018 to 2020, similar proportions of STEC O26 and STEC O157 cases reported diarrhoea (91% versus 91%, p=0.823) and hospitalization (28% v 32%, p=0.263). STEC O26 can be identified by GBRU at

an earlier stage than other non-O157 serogroups associated with severe disease through an O26-specific PCR assay. Incorporating this result into the public health guidance ensures earlier public health action, as O26 is more likely than other higher risk STEC to be associated with severe disease in the presence of an stx1/eae profile (32).

Rationale for public health action

Human infection with STEC is predominantly acquired through the consumption of contaminated foods, with several large-scale foodborne outbreaks documented in the published literature. Person-to-person spread within household and nursery settings has also been well documented and there is evidence that younger children, particularly those aged under 6 years and attending nursery or other childcare settings, are at an increased risk of both developing severe infection and facilitating onward transmission (6, 66).

What is less well-documented, however, is evidence of outbreaks in settings involving secondary transmission amongst other risk group populations, such as healthcare workers or food handlers.

The increased incidence of STEC infections in children may, in part, reflect enhanced detection of cases in this group, due to a greater likelihood that medical advice may be sought for younger children with diarrhoeal symptoms. It may also reflect an increase in risk factors for developing gastrointestinal illnesses within this cohort, such as inadequate personal hygiene habits (66). In contrast, it is more likely – although not inevitable – that adults in risk groups such as food handling, caring or healthcare roles will have increased levels of hand hygiene and access to handwashing facilities to help prevent the onward transmission of gastrointestinal illness.

To help support the development of the recommendations in these guidelines, guidelines on the management of STEC infections and HUS in Western countries other than the UK were reviewed (62, 67 to 74). Although the public health management of cases and contacts of STEC or HUS varies between regions, the majority of guidelines support the exclusion and/or microbiological screening of cases in children. However, the management of cases and contacts within other risk groups is less standardised, with guidelines including the use of measures to redeploy or restrict staff within these settings.

This guidance aims to protect those groups at greatest risk of developing severe illness and facilitating onward transmission, while taking a pragmatic approach to supporting those for whom the risk of onward transmission appears to be lower. As such, these guidelines stress the importance of focussing public health actions on children aged 5 years old and under, whilst facilitating health protection teams to carry out detailed risk assessments for those in other risk groups – to establish whether restrictions to working patterns or redeployment to other roles may be possible. Where this approach is not feasible, the guidelines stress the need to focus on protecting public health via exclusion and microbiological testing methods as required.

Microbiological diagnosis

Recommended procedures for the investigation of diarrhoea by diagnostic/diagnostic laboratories are detailed in the UK ‘Standards for Microbiology Investigations: Investigation of faecal specimens for enteric pathogens’ (1).

As described, specific procedures used by diagnostic laboratories may vary, however most will carry out a morphological identification, a slide agglutination (or latex kit) test and a biochemical test to identify the organism.

When all 3 procedures have been completed and are positive, this may be referred to in laboratory terms as presumptive (locally confirmed) isolate which satisfies the following conditions:

- positive typical colony morphology on appropriate selective medium
- positive O157 (by slide agglutination or latex kit)
- positive biochemical identification of *E. coli*

It should be noted that the term ‘presumptive (locally confirmed) isolate’ refers to laboratory isolates only, and not human cases. Refer to Table 1 for definitions of human cases of STEC infection based on laboratory, clinical and epidemiological information.

PCR methods for the detection of Shiga toxin (*stx)* are increasingly used by diagnostic laboratories for the identification of STEC infections. The use of PCR methods has made a significant impact on the ability to identify and estimate the burden of STEC infections caused by non-O157 serotypes. Where diagnostic laboratories report PCR positive, culture negative results, this may reflect numbers of organisms below detection limits for culture measures or the presence of organisms that are non-culturable by diagnostic laboratory methods, including non-O157 STEC serotypes. The management of these cases is detailed in the main Public Health STEC guidelines.

Referral to the GBRU Reference Laboratory

Diagnostic laboratories should refer specimens to the Gastrointestinal Bacteria Reference Unit (GBRU) following the guidance below :

A) Cases of HUS

1. Laboratories using culture-based methods for detection of STEC should refer faecal specimens from cases of HUS on the day of receipt to GBRU.
2. Laboratories using PCR or EIA for detection of STEC should refer all positive faecal specimens from cases of HUS urgently to GBRU to optimise isolation (non-O157 and STEC O157), characterisation of virulence and typing.
3. Consider sending a serum specimen for detection of antibodies to *E. coli* from the case if culture or PCR results from GBRU are negative.

B) Cases without HUS

1. Presumptive (locally confirmed) isolates of *E. coli* O157 for confirmation of identity, Shiga toxin gene detection and serotyping.
2. Faecal samples testing positive by PCR in local diagnostic laboratories where commercial PCR assays for GI infections are used routinely and are culture negative locally for presumptive *E. coli* O157.
3. Other strains of *E. coli* for confirmation of identity and Shiga toxin gene detection if there is a high clinical suspicion of STEC infection.
4. Faecal specimens from cases with bloody diarrhoea in whom conventional laboratory testing has failed to yield presumptive *E. coli* O157 or any other pathogen.
5. Faecal samples from symptomatic contacts of cases of STEC infection or any STEC outbreak-associated case in whom conventional culture laboratory testing has failed to yield a pathogen. These should be discussed with GBRU prior to submission to ensure there is capacity for testing.

The GBRU sends results to the diagnostic laboratory in paper form but in urgent cases also telephone results. HPTs have access to STEC reports from the GBRU via the Gastro Data Warehouse (GDW2). The diagnostic laboratory should forward all results from the GBRU to their local HPT by telephone. HPTs should be informed irrespective of whether the results are positive or negative for STEC infection.

Appendix C. Accessible text versions of the algorithm

Stage 1. Case presents as either step 1 a, b, c, d or e

Step 1a (see note 2)

Local culture *E. coli* O157 positive or clinical history of HUS or Symptomatic contact with epi link to another case with HUS or higher risk STEC including O157/O26 then implement public health actions 1:

- if HUS and *stx* PCR positive, define as CONFIRMED otherwise define as PROBABLE case follow higher risk STEC management (Section 2 of guidance)
- go to stage 2 (see note 3)

Step 1b

stx PCR positive, local culture *E. coli* O157 negative (see notes 6 and 7).

Question: does the case have HUS or is there an epi link to a case with other higher risk strain (for example, STEC O26)?

If yes, implement public health actions 1:

- if HUS and *stx* PCR positive, define as CONFIRMED otherwise define as PROBABLE case follow higher risk STEC management (section 2 of guidance)
- go to stage 2

If no, go to Step 2.

Question: does the case have diarrhoea or has the case been hospitalised? (See notes 8 and 9)

If yes, implement public health actions 2:

- define as PROBABLE case
- complete STEC questionnaire
- advise diagnostic sample be sent to GBRU
- give hygiene advice and warn further tests being done
- exclude all cases until 48 hours symptom free
- for cases in risk group B start clearance, exclude until GBRU results or clearance achieved, whichever is sooner
- for cases in risk groups A,C or D, carry out risk assessment

- identify linked cases with common exposure
- identify contacts

If no, question: is the case 5 years and under?

If yes, define as POSSIBLE case, send the PCR letter and leaflet to case with copy to GP. Case makes contact with HPT after receiving letter.

If yes, implement public health actions 3 (see note 10).

- define as POSSIBLE case
- contact guardian by phone
- give hygiene advice
- exclude case until 48 hours symptom free
- ask about potential transmission

Step 1c

Case reports bloody diarrhoea or hospitalisation? If yes, go back to public health actions 2:

- define as POSSIBLE case
- contact guardian by phone
- give hygiene advice
- exclude case until 48 hours symptom free
- ask about potential transmission

If no, question: are there symptomatic contacts?

If no, wait for GBRU in-house PCR result, usually available about 8 days after initial frontline laboratory report to HPT or 11 days after original sample collected.

If yes, go to public health actions 3:

- arrange diagnostic sample
- give hygiene advice
- exclude contact until 48 hours symptom free

Step 1d (see note 4)

Symptomatic contact with epi link to another case with potential higher risk strain, go to public health actions 2:

- define as PROBABLE case
- complete STEC questionnaire
- advise diagnostic sample be sent to GBRU
- give hygiene advice and warn further tests being done

- exclude all cases until 48 hours symptom free
- for cases in risk group B start clearance, exclude until GBRU results or clearance achieved, whichever is sooner
- for cases in risk groups A, C or D, carry out risk assessment
- identify linked cases with common exposure
- identify contacts- if risk group B contacts, exclude and screen

Step 1e (see note 5)

Symptomatic contact with epi link to another case with lower risk strain, define as PROBABLE case and go to public health actions 3**:**

- arrange diagnostic sample
- give hygiene advice
- exclude contact until 48 hours symptom free

Stage 2. GBRU in-house PCR result (see note 12)

STEC isolated (STEC PCR:+, culture :+) or stx genes detected (STEC PCR:+ cultures:-). Define as CONFIRMED case.

Question: is the case *eae* positive and STEC isolated? (See note 13)

If no, public heath actions are:

- exclude until 48 hours symptom free
- no further public health action required

If yes, question: is the case *stx2* positive or STEC O26 identified (wait 2 working days)? (See note 14)

If yes, question: has the HPT already begun public health actions? (See notes 15 and 16)

If no, public health actions are:

- exclude until 48 hours symptom free
- no further public health action required

If yes, public heath actions are:

All cases re-enforce hygiene advice, complete STEC questionnaire if not already done, seek evidence of transmission HUS/probable *E. coli* O157/STEC O26:

- complete all actions for cases and contacts per higher risk STEC management (section 2)

- bloody diarrhoea:
- case in risk group A,C,D initiate clearance samples
- risk group B (regardless of bloody diarrhoea):
- continue clearance samples and continue exclusion until cleared

Question: is there evidence of transmission?

If no, no further public health action required with contacts.

If yes, review both case and contacts and route of transmission. Wait for GBRU stx subtyping information, usually available about 16 days after initial frontline laboratory report to HPT or 21 days after original sample taken.

Go to Stage 3.

If, no (see note 17) and question: is there evidence of transmission? Or is the case aged 5 years and under? Or STEC O26?

If yes, exclude until 48 hours symptom free:

- case in risk group initiate clearance samples
- exclude and screen asymptomatic contacts in risk group B, unless risk assessment supports screening without exclusion
- manage symptomatic contacts as ‘probable’ cases and complete STEC questionnaire
- identify cases linked by common exposure

If no:

- exclude until 48 hours symptom free
- no further public health action required

And wait for GBRU *stx* subtyping information, usually available about 16 days after initial frontline laboratory report to HPT or 21 days after original sample taken. Go to stage 3.

Stage 3: GBRU WGS result define as CONFIRMED case

Question: Does the STEC belong to a higher risk strain? (See note 19)
If no (see note 20), question: has GBRU advised that serotype has other markers eg aggR or is a serotype of concern?

If no, no further action.

If yes, question: has the HPT already begun public health actions?

If no, complete the STEC questionnaire:

- reinforce hygiene advice and move to step 2

If yes, question: is there evidence of transmission or is the case aged 5 years and under? (See notes 22 and 23)

If no, update risk assessment.

If yes, check all public health actions completed. (See notes 21 and 24)

Step 2 (see note 25)

Question: is there evidence of transmission?

If yes:

- exclude until 48 hours symptom free
- risk assess both case and contacts and route of transmission
- consider seeking expert opinion to decide proportionate screening or clearance and exclusion strategy

If no, move to next question. (see note 26)
Question: is the case aged 5 years and under?

If yes:

- exclude until 48 hours symptom free
- risk assess both case and contacts and route of transmission
- consider seeking expert opinion to decide proportionate screening or clearance and exclusion strategy

If no, no further public health action required.

End of accessible text for the 3 algorithms.

References

1. Standards Unit PHE. 'UK Standards for Microbiology Investigations: Investigation of faecal specimens for enteric pathogens.' 2014. (Accessed 17 January 2017)
2. 'Public Health (Control of Disease) Act 1984 (amended 17 Nov 2017).' England
3. 'Health Protection (Local Authority Powers) Regulations 2010.' England
4. 'Health Protection Regulations 2010 Toolkit. PHE, Lewes District Council, CIEH. July 2011 (revised 2015)'
5. Carroll KJ and others. 'Shiga toxin-producing *Escherichia coli* diagnosed by Stx PCR: assessing the public health risk of non-O157 strains.' European Journal of Public Health 2021: volume 31, issue 3, pages 576 to 582
6. Dabke G and others. 'Duration of shedding of Verocytotoxin-producing *Escherichia coli* in children and risk of transmission in childcare facilities in England.' Epidemiology and Infection 2014: volume 142, issue 2, pages 327 to 334
7. Ihekweazu C and others. 'Large outbreak of verocytotoxin-producing *Escherichia coli* O157 infection in visitors to a petting farm in South East England.' 2009. Epidemiology and Infection 2012: volume 140, issue 8, pages 1,400 to 1,413
8. Desai M and others. 'Factors associated with prolonged *Escherichia coli* O157 infection in a school outbreak.' Public Health 2013: volume 127, issue 6, pages 582 to 585
9. Miliwebsky E and others. 'Prolonged fecal shedding of Shiga toxin-producing *Escherichia coli* among children attending day-care centers in Argentina.' Revista Argentina de Microbiología 2007; volume 39, issue 2, pages 90 to 92
10. Tourdjman M and others. 'Duration of shedding and secondary household transmission of Shiga toxin-producing *Escherichia coli* O26 during an outbreak in a childcare center.' Oregon, October to December 2010. Journal of Pediatric Infectious Diseases Society 2012: volume 1, issue 4, pages 329 to 332
11. Brown JA and others. 'Outbreak of Shiga toxin-producing *Escherichia coli* serotype O26: H11 infection at a child care center in Colorado.' Pediatric Infectious Diseases Journal 2012: volume 31, issue 4, pages 379 to 383
12. MacDonald E and others. 'Implications of screening and childcare exclusion policies for children with Shiga toxin-producing *Escherichia coli* infections: lessons learned from an outbreak in a daycare centre, Norway, 2012.' BMC Infectious Diseases 2014: volume 14, page 673
13. Vonberg RP and others. 'Duration of fecal shedding of Shiga toxin-producing *Escherichia coli* O104:H4 in patients infected during the 2011 outbreak in Germany: a multicenter study.' Clinical Infectious Diseases 2013: volume 56, issue 8, pages 1,132 to 1,140
14. Wahl E and others. 'Investigation of an *Escherichia coli* O145 outbreak in a child day-care centre: extensive sampling and characterization of eae- and stx1-positive *E. coli* yields epidemiological and socioeconomic insight.' BMC Infectious Diseases 2011: volume 11, page 238

15. Collins A and others. 'A 10-year analysis of VTEC microbiological clearance times, in the under-6 population of the Midlands, Ireland.' Epidemiological Infections 2017: volume 145, issue 8, pages 1,577 to 1,583
16. Matussek A and others. 'Shiga toxin-producing *Escherichia coli* in diarrheal stool of Swedish children: evaluation of polymerase chain reaction screening and duration of Shiga toxin shedding.' Journal of Pediatric Infectious Diseases Socicety 2016: volume 5, issue 2, pages 147 to 151
17. Pihkala N, B.N., Eblen D, Evans P, Johnson R, Webb J, Williams C and the FISS non-O157 working group. 'Risk profile for pathogenic non-O157 Shiga toxin-producing *Escherichia coli* (non-O157 STEC).' May 2012, Office of Public Health Science, Office of Policy and Program Development, Food Safety and Inspection Service, United States Department of Agriculture
18. Rangel JM, S.P., Crowe C and others. 'Epidemiology of *Escherichia coli* O157:H7 outbreaks, United States 1982 to 2002.' Emerging Infectious Diseases 2005: volume 11, issue 4, pages 603 to 609
19. World Health Organization (WHO). *E. coli* fact sheet. October 2016 (cited 1 February 2017)
20. Smith KE and others. 'Quinolone-resistant *Campylobacter jejuni* infections in Minnesota, 1992 to 1998.' Investigation Team. New England Journal of Medicine 1999: volume 340, issue 20, pages 1,525 to 1,532
21. WHO Factsheet: Campylobacter. 2020 (accessed 24 September 2021)
22. Harris NV and others. 'Dairy products, produce and other non-meat foods as possible sources of *Campylobacter jejuni* and *Campylobacter coli* enteritis.' Journal of Food Protection 1986: volume 49, issue 5, pages 347 to 351
23. Harris NV, NS Weiss and CM Nolan. 'The role of poultry and meats in the etiology of *Campylobacter jejuni/coli enteritis*.' American Journal of Public Health 1986: volume 76, issue 4, pages 407 to 411
24. Tokuda K, Y Yahata and T Sunagawa. 'Prevention of secondary household transmission during Shiga toxin-producing *Escherichia coli* outbreaks.' Epidemiology and Infection 2016: volume 144, issue 14, pages 2,931 to 2,939
25. Byrne L and others. 'Epidemiology and microbiology of Shiga toxin-producing *Escherichia coli* other than serogroup O157 in England, 2009 to 2013.' Journal of Medical Microbiology 2014: volume 63, issue 9, pages 1,181 to 1,188
26. Rahal EA, K.N., Nassar FJ, Matar GM. '*Escherichia coli* O157:H7: clinical aspects and novel treatment approaches.' Frontiers in Cellular and Infection Microbiology 2012: 2
27. Launders N and others. 'Disease severity of Shiga toxin-producing *E. coli* O157 and factors influencing the development of typical haemolytic uraemic syndrome: a retrospective cohort study, 2009 to 2012.' BMJ Open 2016. doi:10.1136/bmjopen-2015009933
28. Freedman SB, X.J., Neufeld MS, Hamilton WL, Hartling L, Tarr PI. Alberta Provincial Pediatric Enteric Infection Team (APPETITE). 'Shiga toxin–producing *Escherichia coli* infection, antibiotics, and risk of developing Hemolytic Uremic Syndrome: a meta-analysis.' Clinical Infectious Diseases 2016: volume 62, issue 10, pages 1,251 to 1,258

29. Johnson KE, CM Thorpe and CL Sears. 'The emerging clinical importance of non-O157 Shiga toxin-producing *Escherichia coli*.' Clinical Infectious Diseases 2006: volume 43, issue 12, pages 1,587 to 1,595
30. Brooks JT and others. 'Non-O157 Shiga toxin-producing *Escherichia coli* infections in the United States, 1983 to 2002.' Journal of Infectious Diseases 2005: volume 192, issue 8, pages 1,422 to 1,429
31. Scheutz F. 'Taxonomy meets public health: the case of Shiga toxin-producing *Escherichia coli*.' Microbiology Spectrum 2014: volume 2, issue 3
32. Vishram B and others. "The emerging importance of Shiga toxin-producing *Escherichia coli* other than serogroup O157 in England.' Journal of Medical Microbiology 2021: volume 70, issue 7
33. EFSA Panel on Biological Hazards (BIOHAZ). 'Scientific opinion on VTEC-seropathotype and scientific criteria regarding pathogenicity assessment.' EFSA Journal 2013: volume 11, issue 4, page 3,138
34. Frank C anf others. 'Epidemic profile of Shiga toxin-producing *Escherichia coli* O104:H4 outbreak in Germany.' New England Journal of Medicine 2011: volume 365, issue 19, pages 1,771 to 1,180
35. McFarland N and others. 'Recurrent seasonal outbreak of an emerging serotype of Shiga toxin-producing *Escherichia coli* (STEC O55:H7 Stx2a) in the south west of England, July 2014 to September 2015.' Eurosurveillance 2017: volume 22, issue 36
36. Bruyand M and others. 'Major shift in Shiga toxin-producing *Escherichia coli* serogroups causing haemolytic uraemic syndrome in children in France, 1996 to 2015.' Poster presented at: ESCAIDE 28 to 30 November 2016, Stockholm, 2016
37. Soysal N and others. 'Enterohemorrhagic *Escherichia coli* hybrid pathotype O80:H2 as a new therapeutic challenge.' Emerging Infectious Diseases 2016: volume 22, issue 9, pages 1,604 to 1,612
38. Kaspar C, E.D.M., Archer J. 'White paper on non-O157:H7 Shiga toxin-producing *E.coli* from meat and non-meat sources.' December 2009-April 2010. Food Research Institute (Funded in part by the American Meat Institute Foundation): UW-Madison
39. von Muffling T and others. 'Preliminary study of certain serotypes, genetic and antimicrobial resistance profiles of verotoxigenic *Escherichia coli* (VTEC) isolated in Bosnia and Germany from cattle or pigs and their products.' International Journal of Food Microbiology 2007: volume 117, issue 2, pages 185 to 191
40. van Elsas JD and others. 'Survival of *Escherichia coli* in the environment: fundamental and public health aspects.' The ISME journal 2011: volume 5, issue 2, pages 173 to 183
41. Miko A and others. 'Assessment of Shiga toxin-producing *Escherichia coli* isolates from wildlife meat as potential pathogens for humans.' Applied and Environmental Microbiology 2009: volume 75, issue 20, pages 6,462 to 6,470
42. Frank C and others. 'Cattle density and Shiga toxin-producing *Escherichia coli* infection in Germany: increased risk for most but not all serogroups.' Vector Borne Zoonotic Diseases 2008: volume 8, issue 5, pages 635 to 643

43. Hawker J, Begg N, Blair I, Reintjes R, Weinberg J and Ekdahl K. 'Section 3.26 *Escherichia coli* 0157 (and other *E. coli* gastroenteritis), in 'Communicable Disease Control and Health Protection Handbook' 2012. Blackwell Publishing: Chichester
44. Snedeker KG, S.D., Locking ME, Prescott RJ. 'Primary and secondary cases in *Escherichia coli* O157 outbreaks: a statistical analysis.' BMC Infectious Diseases 2009: 9
45. Ferens WA, H.C. '*Escherichia coli* O157:H7: animal reservoir and sources of human infection.' Foodborne Pathogens and Disease 2011: volume 8, issue 4, pages 465 to 487
46. Peron E and others. 'Early findings in outbreak of haemolytic uraemic syndrome among young children caused by Shiga toxin-producing *Escherichia coli*, Romania, January to February 2016.' Eurosurveillance 2016: volume 21, issue 11, page 30,170
47. European Centre for Disease Prevention and Control/European Food Safety Authority. 'Multi-country outbreak of STEC infection associated with HUS: 5 April 2016.' 2016, ECDC: Stockholm
48. Friesema I, S.G., van der Zwaluw K, Heuvelink A, Schimmer B, de Jager C, Rump B, Briem H, Hardardottir H, Atladottir A, Gudmundsdottir E, van Pelt W. 'An international outbreak of Shiga toxin-producing *Escherichia coli* O157 infection due to lettuce, September to October 2007.' Eurosurveillance 2008: volume 13, issue 50, pages 3,029 to 3,035
49. © E.F.S.A. 'Tracing seeds, in particular fenugreek (*Trigonella foenum-graecum*) seeds, in relation to the Shiga toxin-producing *E. coli* (STEC) O104:H4 2011 outbreaks in Germany and France. 2011
50. Luna-Gierke RE and others. 'Outbreaks of non-O157 Shiga toxin-producing *Escherichia coli* infection: USA.' Epidemiology and Infection 2014: volume 142, issue 11. pages 2,270 to 2,280
51. Hoshina K and others. 'Enterohemorrhagic *Escherichia coli* O26 outbreak caused by contaminated natural water supplied by facility owned by local community.' Japanese Journal of Infectious Diseases 2001: volume 54, issue 6, pages 247 to 248
52. Lee SH, L.D, Craun GF, Beach MJ, Calderon. 'Surveillance for waterborne disease outbreaks, United States 1999 to 2000.' Morbidity and Mortality Weekly Report 2002 volume 51, pages 1 to 28
53. O'Sullivan MB and others. 'Increase in VTEC cases in the south of Ireland: link to private wells?' Eurosurveillance 2008: volume 13, issue 39
54. Ohaiseadha C and others. 'A geostatistical investigation of agricultural and infrastructural risk factors associated with primary verotoxigenic *E. coli* (VTEC) infection in the Republic of Ireland, 2008 to 2013.' Epidemiology and Infection 2017: volume 145, issue 1, pages 95 to 105
55. Report of the E. coli O157 Independent Investigation Committee. Review of the major outbreak of *E. coli* 0157 in Surrey, 2009. An evaluation of the outbreak and its management, with a consideration of the regulatory framework and control of risks relating to open farms. June 2010
56. Kintz, E and others. 'Transmission pathways for sporadic Shiga toxin-producing *E. coli* infections: a systematic review and meta-analysis.' International Journal of Hygiene and Environmental Health 2017: volume 220, issue 1, pages 57 to 67

57. Rivas M, S.-E.S., Rangel J and others. 'Risk factors for sporadic Shiga toxin–producing *Escherichia coli* infections in children, Argentina.' Emerging Infectious Diseases 2008: volume 14, issue 5, pages 763 to 771
58. Centers for Disease Control and Prevention. 'Importance of culture confirmation of Shiga toxin-producing *Escherichia coli* infection as illustrated by outbreaks of gastroenteritis: New York and North Carolina, 2005.' Morbidity and Mortality Weekly Report 2006: volume 55, issue 38
59. Bradley KK and others. 'Epidemiology of a large restaurant-associated outbreak of Shiga toxin-producing *Escherichia coli* O111:NM.' Epidemiology and Infection 2012: volume 140, issue 9, pages 1,644 to 1,654
60. Diercke M and others. 'Transmission of Shiga toxin-producing *Escherichia coli* O104:H4 at a family party possibly due to contamination by a food handler, Germany 2011.' Epidemiological Infections 2014: volume 142, issue 1, pages 99 to 106
61. Carroll KJ and others. 'The epidemiology of Shiga toxin-producing *Escherichia coli* infections in the South East of England: November 2013 to March 2017 and significance for clinical and public health.' Journal of Medical Microbiology 2019: volume 68, issue 6, pages 930 to 939
62. Oregon Public Health Division. Investigation guidelines: Shiga toxigenic *Escherichia coli* (including O157, non-O157 and HUS). July 2015
63. Byrne L, J.C., Launders N, Elson R, Adak GK/ 'The epidemiology, microbiology and clinical impact of Shiga toxin-producing *Escherichia coli* in England, 2009 to 2012.' Epidemiology and Infection 2015: volume 143, issue 16, pages 3,475 to 3,487
64. Sharp JCM, RW, Coia JE, Curnow J, Synge BA. '*Escherichia coli* O157 infection in Scotland: an epidemiological overview.' PHLS Microbiology Digest 1995: volume 12: pages 134 to 140
65. Tam C, VL, Adak B, Bolton E, Dodds J, Cowden J, Evans M, Gray J, Hunter P, Jackson K, Letley L, Neal K, Rait G, Smith G, Smyth B, Tompkins D, van der Es M, Rodrigues L and O'Brien S on behalf of the IID2 Study Executive Committee. The Second Study of Infectious Intestinal Disease in the Community (IID2 Study) Final Report. 2012. Food Standards Agency
66. Willshaw GA, CT, Smith HR, O'Brien SJ, Adak GK. 'Verocytotoxin-producing *Escherichia coli* (VTEC) O157 and other VTEC from human infections in England and Wales: 1995 to 1998.' Journal of Medical Microbiology 2001: volume 50, pages 135 to 142
67. California Department of Public Health. 'Guidance for managing select communicable diseases: Shiga toxin-producing *Escherichia coli* (STEC) and Haemolytic Uremic Syndrome (HUS)' January 2015
68. Environment, K.D.o.H.a. 'Kansas Disease Investigation Guidelines: Shiga toxin-producing E. coli (STEC), including Escherichia coli O157:H7 investigation guideline.' June 2012
69. Washington State Department of Health. 'Shiga toxin-producing Escherichia coli (STEC) (including E. coli serotypes O157:H7 and non-O157)' February 2014
70. New South Wales Government. 'Health, Haemolytic uraemic syndrome (HUS) and Shigatoxigenic E. coli infections (STEC) control guideline.' July 2016

71. Government of Alberta. 'Public Health Notifiable Disease Management Guidelines: Haemolytic uremic syndrome.' October 2015
72. Manitoba Health, H.L.a.S. 'Verotoxigenic Escherichia coli (VTEC) infection reporting and case investigation.' November 2015
73. Government of Alberta. 'Alberta health and wellness public health disease under surveillance management guidelines: *Escherichia coli* verotoxigenic infections' March 2011
74. Ontario Ministry of Health and Long-Term Care. 'Appendix A: Disease-specific chapters-Verotoxin-producing E. coli infection indicator conditions, including Hemolytic Uremic Syndrome (HUS).' March 2017

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

Prepared by: STEC Working Group 2021
For queries relating to this document, please contact: Sooria Balasegaram

Published: January 2023
Publishing reference: GOV-12746